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Prepared by U.C. Luft with contributions by L.G. Myhre, W.K. Coester, J.A. Loeppky, and the technical staff of the Physiology Department. J.K. Conrad, F.M. Mowry, and R.R. Pyle performed the cardiac catheterizations described in Part A.

## A. EVALUATION OF THE SINGLE-BREATH METHOD FOR DETERMINING CARDIAC OUTPUT

### I. Comparison of Simultaneous Determinations of Cardiac Output with the Direct Fick Procedure

In the assessment of physical fitness by observing the respiratory and cardiovascular response to graded exercise, it is desirable to have some measure of cardiac output in addition to measurements of ventilation, gas exchange, heart rate, and blood pressure. Invasive procedures involving arterial and venous sampling, as in the dilution methods, or catheterization of the right heart in the direct Fick procedure, are impractical for routine testing. Of the numerous indirect and non-invasive methods that have been proposed, the single-breath (SB) technique ( 6 ) appears to have great advantage in that it does not require a foreign gas, is of no discomfort to the subject, and can be repeated at short intervals with minimal disturbance of the respiratory pattern at rest and during exercise.

The SB method is based upon Fick's principle which derives cardiac output ($\dot{Q}$), or more strictly pulmonary bloodflow, from the amount ($\dot{V}$) of a given gas (G) taken up ($O_2$) or given off ($CO_2$) by the blood per unit of time and the difference in gas content ($C_G$) between arterial (a) and mixed venous ($\bar{v}$) blood:

$$\dot{Q} = \frac{\dot{V}_G}{Ca_G - C\bar{v}_G} \times 100 \qquad (1)$$

where $\dot{V}$ is in L/min(STPD) and C in ml/100 ml. Whereas $\dot{V}_G$ is readily determined from the mixed expired gas, the SB method derives $Ca_{CO_2}$ and $C\bar{v}_{CO_2}$ indirectly from a series of consecutive determinations of $O_2$ and $CO_2$ in the course of a single prolonged expiration. As will be described below, this concept involves several basic assumptions, the validity and consistency of which cannot be accepted without question. The only previous attempt to validate the single-breath procedure by comparison with one of the direct methods, that has come to our knowledge, is by Gilbert and Auchincloss ( 3 ) who reported on 27 simultaneous measurements

of cardiac output by the single-breath and the dye dilution method. They found a good correlation (R = 0.85), but a rather large standard error of 2.9 L/min. In view of the large coefficient of variation between the dye dilution method and the established direct Fick procedure reported in most comparative studies ( 9 ), it was considered preferable to re-evaluate the single-breath technique against the well-established Fick method. The following investigation was undertaken 1) to ascertain how close an agreement could be obtained between cardiac output determinations with the SB method and simultaneous direct Fick measurements, and 2) to determine to what extent the theoretical assumptions underlying the SB concept were valid.

Procedures:

The subjects (Table A-I) were five male volunteers between 30 and 62 years old, all of whom had performed an exercise test previously to determine their aerobic capacity and had practiced the SB maneuver. All measurements were taken with the subject in the supine position on a fluoroscopy table to which a Schwinn bicycle ergometer was attached (Fig. A-1). A cardiac catheter was introduced under fluoroscopic guidance after cut-down with local anesthesia. An indwelling needle was inserted into the brachial artery on the same side. The subject breathed through a low deadspace, low resistance, unidirectional valve (Lloyd-Collins) and mixed expired air was collected in Douglas bags. A capillary sampling catheter was inserted into the mouthpiece in mid-stream approximately one-inch from the lips for breath-by-breath recording of respiratory gases on an X-Y recorder (Hewlett-Packard) and also on time-base on a Heiland Visicorder using a Med Spect (MS-8) Respiratory Mass-spectrometer (Scientific Research Instruments, Inc.). For the resting measurements expired air was collected for 3 minutes, after recording a single-breath maneuver consisting of a slow, deep exhalation after inspiring deeper than usual. In the second minute, ECG and systemic and pulmonary pressures were recorded on an Electronics for Medicine recording system. In the third minute arterial and mixed venous blood samples were drawn from the catheters and respiration recorded. Immediately after completing the third minute a second SB maneuver was recorded. Subsequently each subject performed from three to five exercise tests of 6 minutes duration at

work loads ranging from 300 to 1050 kpm/min with intervals of at least 10 minutes between each. During the fifth minute of each exercise, blood pressure and ECG were recorded and an SB maneuver obtained immediately before collecting expired air and drawing blood samples as above. Exercise was terminated after recording the second SB maneuver. In this manner a total of 20 determinations were made with the Fick procedure and a corresponding SB determination immediately before and after blood sampling. The procedure was tolerated without incident with the exception of one subject who developed atrial fibrillation while the catheter was being passed through the right heart. Nevertheless, he completed the resting measurements and three levels of exercise without difficulty. The fibrillation persisted for the following 5 hours whereupon normal cardiac activity returned spontaneously.

All blood samples were analyzed for $O_2$ and $CO_2$ content (Van Slyke), $P_{O2}$, $P_{CO2}$, and pH (Corning 16 Electrode system) and hemoglobin content (Instrumentation Laboratories, CO-Oximeter). Expired air was analyzed by the Scholander method and volumes measured by dry gas meter. From these measurements the following information was derived for each of the 20 determinations:

1. Total ventilation, tidal volume, $O_2$ uptake, $CO_2$ output, and RQ
2. Alveolar ventilation
3. Effective ventilation and deadspace ventilation
4. Alveolar $P_{O2}$ and $P_{CO2}$
5. Arterial $P_{O2}$, $P_{CO2}$, pH, bicarbonate and base-excess, $O_2$ content, capacity and saturation
6. The same as item 5 for mixed venous blood
7. Heart rate, arterio-venous $O_2$ and $CO_2$ difference, stroke volume and cardiac output
8. Systemic and pulmonary blood pressures
9. Systemic and pulmonary vascular resistance

The SB maneuvers were recorded and processed by Dr. M. Buderer, NASA MSC, Biomedical Research Division, and programmed for calculation of cardiac output ($\dot{Q}_{SB}$) by computer (Burroughs 5500) at the Lovelace Foundation. (For details of procedure see below.) From these, 28

technically acceptable records were available for comparison with the direct Fick results ($\dot{Q}_F$).

Results:

(a) Cardiac Catheterization Study

The comprehensive metabolic, respiratory, and cardiovascular data obtained on occasion of the validation of the SB method are summarized in Tables A-II through A-IV and Figures A-2 through A-7 because they contain information of general interest to cardiologists and physiologists and provide normal standards for the response to graded exercise in healthy men at an elevation of 5400 ft. Fig. A-2 shows the relationship between cardiac output and metabolic rate. The regression on 20 points is:

$$\dot{Q}_F = 5.17\,\dot{V}_{O2} + 5.99 \qquad (2)$$
$$SE = 1.42 \qquad (\dot{Q}_F \ \mathrm{L/min};\ \dot{V}_{O2}\ \mathrm{L/min})$$

Both the regression and the scatter are in good agreement with those reported for the supine position by several other investigators as summarized by Ekelund and Holmgren ( 2 ). There was no consistent change in stroke volume (Fig. A-3) with increasing energy cost, although four out of five subjects showed a slight increase during exercise. Subject #2, who had atrial fibrillation during the tests, had a considerably smaller stroke volume compared with all the others, but his heart rate was correspondingly higher at comparable work loads (Table A-II). On the other hand, the arterio-venous difference for oxygen (Fig. A-4) increased steadily with rising oxygen consumption in all subjects.

Figures A-5 and A-6 show mean pulmonary arterial pressure and pulmonary vascular resistance versus cardiac output for the individual subjects. The increase in pulmonary pressure was within normal limits ( 2 ) in four subjects, but more marked in Subject #1, who was much older than the others. The latter showed a corresponding increase in pulmonary vascular resistance with higher blood flows in contrast to the other subjects. A consistent reduction in systemic arterial resistance with increasing cardiac output is apparent from Fig. A-7.

(b) Comparison between direct Fick ($\dot{Q}_F$) and Single-Breath Cardiac Output ($\dot{Q}_{SB}$)

There is a good correlation between the two methods (R = 0.92) as shown in Fig. A-8. However, the mean value for $\dot{Q}_{SB}$ is 1.97 L/min (16.2%) lower than for $\dot{Q}_F$, and this difference is statistically highly significant ( $p < 0.001$) as shown in Table A-VI. Moreover, the skewed distribution of the data below the identity line strongly suggests a systematic error in $\dot{Q}_{SB}$ relative to $\dot{Q}_F$. In future studies with the SB method, the regression equation derived from these data can be used effectively to minimize this systematic error by adjusting measured $\dot{Q}_{SB}$ values as follows: By solving the regression equation

$$\dot{Q}_{SB} = 0.78(\dot{Q}_F) + 0.69 \qquad \text{for } \dot{Q}_F \tag{3}$$

$$\dot{Q}_{F'} = 1.28\,\dot{Q}_{SB} - 0.88 \tag{4}$$

an adjusted value is obtained, designated in the following as $\dot{Q}_{F'}$ for predicted $\dot{Q}_F$. Using this calculation, all points in Fig. A-8 have been replotted in Fig. A-9 against the direct $\dot{Q}_F$. The statistics (Table A-V) reveal a mean difference of 0.02 L/min (statistically not significant) and the distribution is now random across the identity line with a standard deviation of the differences that is slightly greater than for $\dot{Q}_{SB}$ (Table A-VI). With this adjustment the difference between $\dot{Q}_{F'}$ and $\dot{Q}_F$ is less than 10% in 13 points (46%), between 10% and 20% in 12 (43%), and more than 20% in only 3 (11%) cases. The standard deviation of differences between the two methods is 13.6%. Although based on a limited number of comparative measurements, this treatment definitely improves the estimate of $\dot{Q}_F$ from $\dot{Q}_{SB}$ at rest and in submaximal exercise.

In order to determine whether the systematic difference in the $\dot{Q}_{SB}$ method is due to the estimation of $P\bar{v}_{CO2}$ and $Pa_{CO2}$ from the single-breath record, or is inherent in the assumptions made in the equation (5) proposed by Kim, et. al. ( 6 ),

$$\dot{Q} = \frac{\dot{V}_{O2}\,(R_E - 0.32)}{4.7\,(P\bar{v}_{CO2} - Pa_{CO2})} \tag{5}$$

the same calculation was made using the direct measurements of $P\bar{v}_{CO2}$ and $Pa_{CO2}$ shown in Table A-III instead of those derived from the SB record. The results of 20 comparisons between $\dot{Q}_F$ and $\dot{Q}_{PCO2}$ are shown

in Fig. A-10 and analyzed in Table A-VI. Here the mean difference is +0.400 L/min (3.3%) and this is not statistically significant. The distribution of differences is entirely random indicating that there is no systematic error involved when blood gases are used instead of alveolar gas measurements. On the other hand, the standard deviation of differences between $\dot{Q}_{PCO_2}$ and $\dot{Q}_F$ is considerably greater (24.9%). In this regard, the adjusted SB method is preferable. Fig. A-11 based on Eq. 3 gives the regression line from which $\dot{Q}_{F'}$ can be read off for any measured $\dot{Q}_{SB}$. Possible reasons for the systematic error between the two methods, which can be minimized by this adjustment, will be discussed in the following section.

## II. Critical Appraisal of Theory and Assumptions Underlying the Single-Breath Method

The fact that arterial and mixed venous blood samples were obtained in close coincidence with the single-breath recordings made it possible not only to validate the cardiac outputs derived from the latter, but also to test the validity of certain assumptions made in the calculations by the originators of the method:

1. Equality of $P_{O_2}$ and $P_{CO_2}$ in the alveolar gas and pulmonary capillary blood at any given phase of the protracted expiration
2. Linearity of the relationship between $P_{CO_2}$ and R in the plot derived from the sequential measurements of $P_{O_2}$ and $P_{CO_2}$ on the $O_2$-$CO_2$ diagram
3. The Haldane effect is a constant, namely 0.32 ml/100 ml $CO_2$ for every ml/100 ml $O_2$ exchanged without change in $P_{CO_2}$ in the blood.
4. A constant slope of 4.7 ml/liter/mm Hg for the $CO_2$ dissociation curve of whole blood

The appraisal of these points will be preceded by a discussion of the procedure employed to obtain the most appropriate points from the single-breath record and attempts to improve it.

During the single-breath maneuver the subject, when given a signal, inspires to a volume between the prevailing tidal volume and vital capacity.

Without pause he exhales, attempting to maintain a constant flow and continuing to expire to residual volume. The mean expiration times during the validation experiments were 15 sec at rest and 8 sec during exercise. Minor variations in the volume inspired prior to, or in flow rate during the protracted expiration apparently do not distort the results. This procedure followed that first described by Kim, et. al. ( 6 ), except that a restrictive orifice was not used here. Preliminary observations indicated that the characteristics of the X-Y curve did not change appreciably when the maneuver was performed with or without an orifice in the expiratory line; thus it was omitted. At higher levels of work the expiration time can be shorter because the arterio-venous difference in the blood gases is greater and a shorter time is required to obtain a representative $\Delta P_{CO_2}/\Delta R$ slope. The course of expired $O_2$, $CO_2$, and $N_2$ during a SB maneuver after normal breathing is shown in Fig. A-13 on the oscillograph and in Fig. A-12 on the X-Y recorder.

Kim, et. al. ( 6 ) obtained serial gas samples during the single expiration after the deadspace portion of the expirate had been washed out. These six or seven points were plotted on $P_{O2}$-$P_{CO2}$ coordinates as in Fig. A-14a. He then drew a smooth curve through these points, rejecting points that deviated more than a prescribed amount from this apparent curve. Tangents were drawn by eye to this curve at the points and these slopes converted to R values by the alveolar equation for $CO_2$ in the inspired air.

$$P_{ACO2} = (P_B - 47) \cdot \frac{RF_{ICO2} + F_{ICO2}}{1 - (1 - R)F_{IO2}} - \frac{R + (1 - R)F_{ICO2}}{1 - (1 - R)F_{IO2}} \cdot P_{AO2} \qquad (6)$$

Because this is an equation of linear form (y = a + bx), the slope of the curve on the $O_2$-$CO_2$ diagram is defined by the coefficient of the $P_{AO2}$ term. Since a curve, not a straight line, results from a prolonged expiration, any coordinate point on this line can be considered an "inspired"

point and the instantaneous R at that point can be computed by rearranging the coefficient term if one has the slope value.

$$\frac{\Delta P_{ACO2}}{\Delta P_{AO2}} = - \frac{R + (1-R)F_{ICO2}}{1-(1-R)F_{IO2}} = b \tag{7}$$

Letting $\Delta P_{ACO2}/\Delta P_{AO2}$ (the tangent to the curve at any point defined by $F_{O2}$, $F_{CO2}$ in Fig. A-14a) be equal to b and rearranging

$$R = \frac{b-(F_{IO2}\cdot b)-F_{ICO2}}{1-(F_{IO2}\cdot b)-F_{ICO2}} \tag{8}$$

Kim plotted the calculated R values (X-axis) against the corresponding $P_{CO2}$ values and found this relationship to be linear (Fig. A-14b). He determined this slope by eye and the blood gas tensions were obtained at R = 0.32 for mixed venous blood and at the R of mixed expired gas for arterial. A modification of the Fick equation given above (Eq. 5) is then used to calculate cardiac output ($\dot{Q}_{SB}$).

The slopes obtained at various points to the curve presented in Fig. A-14a are crucial to the final $\dot{Q}$ estimate and the latter is very sensitive to the former. Therefore, it appeared desirable to obtain an equation for the smoothly curved portion of the curve (B to C, Fig. A-12). The first derivative of such an equation would then be the tangent to it at any selected point. For the validation study, four $\dot{Q}$ calculations were programmed and, based on the best comparison with the Fick results, one computational program was retained. For each of these computations, eight points were read off the curve between B and C of Fig. A-12. The points were not selected equidistantly on any axis, but covered the major portion of this curve. If the curvature was not smooth, more points were selected in that area of the curve where the maximum curvature was apparent. The four computations of $\dot{Q}$ from the same data points were as follows:

1. A quadratic fit to the data points using the method of least squares, assuming all error to be in $y(P_{CO2})$

2. Same as (1) but rejecting any of eight points that have a computed R less than 0.30 or greater than a 1.0 value
3. An exponential fit to the data points
4. Same as (3) but rejecting points similarly to (2)

All four computations were programmed to not accept points with $P_{CO2}$ values less than 30 mm Hg, and to reject the entire calculation if the range of computed R was less than 0.2 or if less than four points remained. From the five subjects, 34 single-breath recordings were obtained at rest and exercise, with two single-breath curves corresponding to each $\dot{Q}_F$ determination. Six of these had been discarded in the validation study (Section I) for technical reasons, but were included in this analysis. When each of these four $\dot{Q}_{SB}$ values were compared to the corresponding $\dot{Q}_F$ computation, method (4) gave the closest answer 42% of the time and method (1) 34%. When the closest $\dot{Q}_{SB}$ of each pair of $\dot{Q}_{SB}$ values was considered, method (1) was closest 37% and method (4) 32% of the time. However, method (4) rejected the entire run 18 times out of the 38 recordings, whereas method (1) only rejected one recording. Based on this high mortality for method (4), method (1), the quadratic fit, was temporarily adopted as the method of choice and was subsequently improved. Without further modification, this method gave a mean percent error of -12.6% and a percent error of 25.1%. The percentage error was in all cases computed as follows:

$$\% \text{ error} = \frac{\dot{Q}_{SB} - \dot{Q}_F}{\dot{Q}_F} \times 100 \qquad (9)$$

The $P_{CO2}$ values that were recorded during the single expiration were lower here in Albuquerque (elevation: 5400 ft.) than those found at sea level. This apparent altitude effect resulted in many of the $\dot{Q}_{SB}$ being computed with less than 8 points because the program was to reject points with $P_{CO2}$ values less than 30 mm Hg. This restriction was removed to gain consistency, meaning that 8 points were considered in each computation. The other criteria of rejection, that of not computing the $\dot{Q}$ when the span of R was less than 0.2, was also removed. The latter restriction had resulted in only one $\dot{Q}_{SB}$ not being computed. A repeat run on the same data points with these restrictions removed gave a mean percent

error of -12.6%, the same as before, but the standard deviation was reduced slightly to a 23.0% value. The $P_{CO_2}$ restriction had been introduced initially because the slope of the $CO_2$ dissociation curve, considered a constant in the calculation for $\dot{Q}$, is known to deviate increasingly from linearity at $P_{CO_2}$ values of 30 to 35 mm Hg ( 6 ). The restriction resulted in points being eliminated from the lower end of the curve (near point B in Fig. A-12 ). Removing this restriction resulted in the same mean percent error even though now points as low as 23.4 mm Hg ($F_{CO_2}$ = .0401) were being considered for any given curve.

Further mathematical considerations and trial-and-error manipulations made it apparent that the form of the quadratic equation which was computed to approximate the curve, i.e., the constants of $y = A + Bx + Cx^2$ was extremely dependent on where the points were chosen from the X-Y curve and also how far down they were chosen on the $CO_2$ axis. It also became apparent that a better approximation of the X-Y plot was achieved from the equation if more points were chosen. Differences of $\dot{Q}_{SB}$ in the range of 20% were obtained by choosing different points or adding more points. These findings resulted in formulation of the following criteria to improve objectivity and reliability in selecting points from the curve. Hopefully these criteria would eliminate some of the error in $\dot{Q}_{SB}$ resulting from inconsistency in point selection.

1. The number of points selected was increased from 8 to 11.
2. These points were chosen equidistant on the $O_2$ axis.
3. The points were chosen on the smooth portion of the curve (between B and C in Fig. A-12 .
4. The last point read was chosen to be at the upper end of the curve (point C).
5. The first point read was where the curve began to curve smoothly to the left. However, if this occurred below a $P_{CO_2}$ of 25.0 mm Hg ($F_{CO_2}$ = .0425), then the latter was used as a lower cut-off.
6. The interval on the X-axis spanned by these two points was divided into 10 equal intervals to the nearest .0005 in $F_{O_2}$ and points taken between the intervals.
7. If irregularities occurred in this portion of the X-Y plot, either due to the heart beat or electrical interference, this portion of the curve

was smoothed over with a french rule and this "interpolated" point was taken from the drawn line.

Of the 34 prolonged expirations, the mean of the points selected at the lower end of the curve was at $F_{O_2} = 0.1628$ and $F_{CO_2} = 0.0464$, while the mean upper end point of the curves was at $F_{O_2} = 0.1115$ and $F_{CO_2} = 0.0714$, giving a mean span of 0.0513 for $F_{O_2}$ ($\Delta P_{O_2} = 29.9$ mm Hg) and a mean span of 0.0251 for $F_{CO_2}$ ($\Delta P_{CO_2} = 14.6$ mm Hg). When each of the same single-breath curves were "re-read" as described above, the new $\dot{Q}_{SB}$ values from the new quadratic fit gave a mean percent error of -17.2%, and a standard deviation of 15.2%. Thus, the new method of selecting the points caused $\dot{Q}_F$ to be further underestimated; however, the scatter of the points around the mean was considerably reduced. Presumably this improvement resulted from the more systematic manner in which the points were chosen.

One advantage of applying the quadratic fit to the data points was that the curve was then numerically defined by considering the constants in the equation ($y = A + Bx + Cx^2$). Also, it made the slope determination operationally simple since $dy/dx = B + 2Cx$ and made possible the determination of $\dot{Q}$ at each point such that a "ventilation-perfusion line" ( 8 ) could be approximated. The amount of curvature at any point on the X-Y plot was found to be directly related to $\dot{Q}$ at that point. Another advantage of the quadratic fit method was that it allowed us to calculate the effect of a drift in calibration. Initially it had been assumed that the large percentage errors in certain single-breaths were the result of large shifts in calibration, especially on the $O_2$ axis because the pen was as much as 7 mm Hg in $P_{O_2}$ to the left (Fig.A-14a) of the inspired air point on a few determinations just prior to the single-breath maneuver. If one assumed that the $P_{O_2}$ shift remained constant throughout the $P_{O_2}$ span, then the computations can be performed that are given in an example in the appendix.

The main disadvantage of the quadratic equation was that it forced $P_{CO_2}$ values to fit into a smooth curve and it was these "smoothed" $P_{CO_2}$ values that were used in the computations of $\dot{Q}_{SB}$. The deviations of the predicted $P_{CO_2}$ from that actually observed from the X-Y plot were computed for the 11 points from each curve. When these 34 means were averaged, the mean deviation was 0.093 mm Hg, the range being 0.02 to

0.34 mm Hg for any given X-Y curve. Although these deviations are small, they may cause considerable deviation in the final $\dot{Q}_{SB}$ calculation. The other disadvantage of one quadratic fit to all the data points is that the R vs $P_{CO2}$ relationship becomes curved because of the equations involved, when in actual fact, it may not be curved, i.e., the quadratic fit procedure introduces this artificial curvature.

A curve-fitting procedure, called the "moving spline" method ( 5 ) was modified ( 1 ) and applied to the same 11 points of each plot. The "spline" procedure has been outlined in the appendix. This mathematical method smoothed the original data somewhat, but did not obscure irregularities as much as did the quadratic fit. The resulting slopes and calculated R values were thus "truer" in relation to the original X-Y curve. The mean deviation in predicted and actual $P_{CO2}$ values was now 0.046 mm Hg (range: 0.00 to 0.14) which is half the value resulting from the quadratic fit. Another advantage of this "spline" computation was that it did not introduce artificial curvature into the R-$P_{CO2}$ relationship. Statistically this method was slightly better than the others listed in Table A-VII, giving a mean % error and a SD of % error of -14.4% amd 17.6%, respectively. The mean standard error of the estimate on the straight line fit to the 9 data points of each R vs $P_{CO2}$ curve (the first and last points were omitted in each case) was 0.60 mm Hg (range: 0.17 to 1.86) when all 34 curves were considered. It is of interest to note that Gilbert, et. al. ( 3 ) accepted all R vs $P_{CO2}$ curves that had a standard error less than 2.00 mm Hg and had to reject many on this basis. A comparison of the percent errors between the $\dot{Q}_F$ and $\dot{Q}_{SB}$ using different criteria in selecting points on the curve for the quadratic equation (1-3) and using the moving spline technique (4) is shown in Table A-VII. The results of this analysis prompted us to adopt the "moving spline" curve-fitting technique, using the point selection criteria mentioned above, as the method of choice.

Subsequently the 28 tests used in Fig. A-8 that had originally been calculated with the quadratic equation were recalculated using the "moving spline" procedure by computer, and the correlation with $\dot{Q}_F$ established:

$$\dot{Q}_{SB}^{sp} = 0.85\,\dot{Q}_F - .47 \qquad r = .94 \qquad SE = 1.23\ L/min \qquad (10)$$

The individual data are presented on Table A-VIII and summarized on Table IX. It is apparent that this treatment actually increased the systematic difference from $\dot{Q}_F$ as compared to $\dot{Q}_{SB}$ in Table A-VI, but reduced the standard deviation of $\Delta\%$. Thereupon the same adjustment was applied as previously to eliminate the systematic error, this time solving Eq. 10 for $\dot{Q}_F$ to obtain

$$\dot{Q}^{sp}_{F'} = 1.18\,\dot{Q}^{sp}_{SB} + .553 \tag{11}$$

The results shown in the last column on Table A-VIII, plotted in Fig. A-15, and summarized in Table A-IX indicate that this treatment not only eliminates the bias in the original data but also reduces the scatter of the data so that more than 2/3 of the points fall within 10% error and only 2 points are more than 20% off. It stands to reason that the application of the "moving spline" technique to describe the single-breath curve and adjusting the $\dot{Q}_{SB}$ calculated according to Kim, et. al. ( 6 ) with Eq. 8 will provide the best results *in future use of the method.*

Alveolar versus blood $P_{CO2}$ and the $P_{CO2}/R$ relationship

Without exception carbon dioxide pressure was higher in both arterial and mixed venous blood as measured directly than estimated from the SB record (Table A-X). However, the mean difference in 28 comparisons was 5.5 mm Hg for the arterial and only 3.6 mm Hg on the mixed venous side and both of these differences were statistically highly significant ($p < .001$). The mean venous-arterial difference in $P_{CO2}$ was 10.3 mm Hg for the blood and 12.2 mm Hg for the indirect determinations. Since this difference is a factor in the denominator of the modified Fick equation (Eq. 5), it follows that $\dot{Q}_{SB}$ estimated in this manner will be smaller than calculated from blood gas measurements, and this is probably the main reason for the systematic difference between the two methods pointed out in Section I. In Fig. A-15 the mean values for arterial and mixed venous $P_{CO2}$ are plotted against R following the scheme in Fig. A-14b. The R value for arterial blood ($R_B$) was calculated as

$$R_B = \frac{C\bar{v}_{CO2} - Ca_{CO2}}{Ca_{O2} - C\bar{v}_{O2}} \tag{12}$$

All blood gas contents were determined by the Van Slyke manometric method. For mixed venous blood ($R_H$) was estimated from the difference in $CO_2$ content between the mixed venous blood and the point on the arterial $CO_2$ combining curve where $P_{CO2}$ is equal to mixed venous $P_{CO2}$ (see Fig. A-17). This difference divided into the arterio-venous difference for oxygen provides $R_H$. As proposed by Kim, et. al. ( 6 ), the R values on the single-breath were taken from the mixed expired air ($R_{\bar{E}}$) for the arterial and a constant, $R_H = 0.32$, used for the mixed venous point.

There is a considerable disparity between the blood and SB lines not only in $P_{CO2}$ but also in R at both ends (Fig. A-16). But the essential point is that the SB line has a considerably greater slope than the blood line, and therefore the arterio-venous difference in $P_{CO2}$ is greater. Only if these lines were truly parallel could the SB method for cardiac output be expected to be equal to results by the direct Fick, whereby the absolute values for $P_{CO2}$ need not necessarily be identical.

The slope of the $CO_2$ combining curve and $R_H$

In the modified Fick equation (5) employed by Kim, et. al. ( 6 ), to estimate cardiac output, a constant of 4.7 ml/liter/mm Hg (.47 vol%/mm Hg) is used to define the slope of the average $CO_2$ combining curve for whole blood. The other constant (0.32) is that respiratory exchange ratio ($R_H$) which is attributable to the amount of $CO_2$ released by the blood for every unit of $O_2$ bound to hemoglobin without change in $P_{CO2}$ due to the Haldane effect. The blood gas analyses performed on the arterial and mixed venous samples by cardiac catheterization enabled us to determine both the slope of the $CO_2$ combining curve and the value for $R_H$ for each of the 20 tests shown on Table A-XI and summarized for the mean values in Fig. A-17. In each case an arterial $CO_2$ combining curve was drawn through the arterial point shown on Fig. A-17, whereby the slope was calculated in terms of $\Delta C_{CO2}/\Delta P_{CO2}$ with the equation given by Peters, et. al. ( 7 ), for the range 30-60 mm Hg $P_{CO2}$:

$$\text{Slope} = 0.0163\,\text{Hb} + 0.21 \qquad (13)$$

The mixed venous point was then plotted and a vertical dropped onto the arterial line to determine the point where arterial and mixed venous $P_{CO2}$

are supposed to become equal in the SB maneuver. The difference in $CO_2$ content at the mixed venous point gives the amount of $CO_2$ released without change in $P_{CO_2}$ (Haldane effect). This $CO_2$ difference divided by the arterio-venous $O_2$ difference constitutes $R_H$. The mean value for the latter was 0.26 as compared to 0.32 adopted by Kim, et. al. ( 6 ), but there was considerable variation (SD: .08). $R_H$ would be expected to change inversely with the slope of the $CO_2$ combining curve, because a steeper slope due to increased hemoglobin content will bring the point where $Pa_{CO_2}$ = $P\bar{v}_{CO_2}$ closer to the mixed venous point and $R_H$ will become smaller. Hemoglobin content increased consistently in the course of the progressive bouts of exercise from a mean resting value of 16.2 g% to 18.0 g% during the last exercise. In spite of this, $R_H$ was generally higher with increasing work loads with an average of 0.17 at rest and 0.31 during the last exercise.

The mean value for the slope of the $CO_2$ combining curve was .49 vol%/ mm Hg, which is slightly higher than the value of .47 used by the originators of the SB method. But this can be accounted for by the higher mean hemoglobin concentration found in this study. At rest, where hemoglobin concentration was on the average 16.2 g%, the slope was 0.47. During the most vigorous exercise the slope was calculated to be .503 vol%/mm Hg corresponding to 18.0 g% Hb.

## III. Discussion

As recently emphasized by Hlastla, et. al. ( 4 ), the cardiac output calculated by the SB method is critically dependent upon the slope of the $P_{CO_2}$ - R relationship (Figs. A-14b, A-16) and its linearity. The latter might be jeopardized if recirculation occurred before the end of the prolonged expiration or if arterial oxygen saturation declined substantially, resulting in a shift in the $CO_2$ combining curve. As can be seen in the example in Fig. A-13, the alveolar $P_{O_2}$ drops as $P_{CO_2}$ rises during expiration. At the end-point the oxygen concentration is 13.1%, which at the elevation of Albuquerque corresponds to a $P_{O_2}$ of 76 mm Hg. If this were to reflect the conditions in the pulmonary capillaries, the oxygen saturation would still be 95%. Granted, during strenuous exercise oxygen pressure can drop considerably further. Thus in some of the experiments a $P_{O_2}$ as low as 55 mm Hg was measured at the end of the SB. This would correspond to 89% $O_2$ saturation, a reduction of about 5% from the arterial level prior to the SB. However, the $CO_2$ combining

curve would not be altered by more than 0.3 vol% and the effect on the $P_{CO_2}$-R relationship would be very small. Nevertheless, a rigorous computer analysis was made of all $P_{CO_2}$-R plots obtained from the original records by the "moving spline" procedure (appendix) using different curve fitting techniques. Although there was some indication of curvilinearity in many of the records, particularly during heavy exercise and with longer expiration times, there was no conclusive statistical evidence of significant departure from linearity.

The most striking finding in this study was the discrepancy between the $P_{CO_2}$-R relationship derived from the SB records and those from direct blood gas analyses. Without exception $P_{CO_2}$ values in the blood were higher than in the gas phase, and this difference was statistically highly significant for the mean differences (Table A-X). Moreover, the difference between the blood and gas values for $P_{CO_2}$ were much greater for the arterial than for the mixed venous ones, and this was associated with a substantially greater slope for the single-breath $P_{CO_2}$-R line (Fig. A-16). In consequence, the venous-arterial difference for $P_{CO_2}$ was significantly ($p < .01$) greater on the SB line than on the blood, with a corresponding underestimate of cardiac output as pointed out above. There are several possible reasons for the unexpectedly large capillary-alveolar gradients. The presence of sequential emptying of alveoli with greater contribution from well-ventilated alveoli in the early part of expiration might explain the greater differences in the arterial points than on the venous side reflected in the latter part of expiration. The effect of storage of $CO_2$ in lung tissue, discussed by the originators of the method as a possible source of error ( 6 ) could also be invoked here, if it is assumed that the rate of $CO_2$ storage were greater at the beginning than at the end of expiration. On the other hand, one would expect the effect of $CO_2$ storage to be less apparent during exercise, because the storage capacity of lung tissue is limited and much larger amounts of $CO_2$ are being transferred through the lungs in physical activity. And yet, the blood-gas $CO_2$ gradients were not consistently smaller during exertion.

A discrepancy was also noted between the R values calculated for the blood and for the mixed expired gas, which is used to determine the arterial point on the SB line (Fig.A-14a). The mean difference shown in this figure is only 0.03, but it is apparent from columns 11 and 12 in Table A-XI that

the differences were much greater at rest and lower levels of exercise than at the highest work load where $R_B$ and $R_{\bar{E}}$ were practically identical. Differences between $R_B$ and $R_{\bar{E}}$ are frequently observed at rest, particularly in patients with ventilation/perfusion inequality where the alveolar-arterial $O_2$ gradients are invariably greater than the arterial-alveolar $CO_2$ gradients because of the different slopes of the dissociation curves for the two gases in the blood. Whether the distribution of $\dot{V}/\dot{Q}$ improved that much with exercise one can only speculate. Certain is that the overall $\dot{V}_A/\dot{Q}$ ratios increased from an average of 1.01 at rest to 3.72 at the heaviest exercise.

Another interesting observation was that $R_H$ values calculated from the blood gases and hemoglobin concentration, which were used as the mean $R_H$ for mixed venous blood in Fig. A-16 and are presented in Table A-XI, col. 10, were on the average lower than the value of 0.32 proposed by Kim, et. al. ( 6 ). It must be borne in mind that the estimation of this term is rather tenuous in vivo because the possible errors of measurement in seven different blood gas determinations and the hemoglobin are involved in its computation (Table A-XI, cols. 1-10). Therefore the coefficient of variation of 33% is not surprising. In spite of the large variation in calculated $R_H$, the mean difference from 0.32 was statistically significant ($p < .01$). Since the individual $R_H$ values were calculated using the actual hemoglobin concentration, one would expect the $R_H$ values to become smaller in exercise, where there was a consistent increase in hemoglobin. The following interrelation between Hb, the slope of the $CO_2$ combining curve, and $R_H$ was calculated using the mean values for arterial and venous blood gases given in Fig. A-17.

| Hb g% | Slope vol%/mm Hg $P_{CO_2}$ | $R_H$ |
|---|---|---|
| 14.0 | .438 | .326 |
| 16.0 | .470 | .280 |
| 18.0 | .503 | .247 |
| 20.0 | .536 | .202 |

In view of this, it is difficult to explain why, according to the data in Table A-XI, col. 10, $R_H$ generally increased with progressive exercise so that in the last stage of exercise the mean value for all subjects was 0.31, actually very close to the value stipulated by the originators of the method. It may have some significance that the changes in $R_H$ (Table A-XI, col. 10) were similar to those of $R_B$ (col. 11) in the course of the tests.

The values calculated for the slope of the $CO_2$ combining curve on the basis of hemoglobin concentration were quite close to .47 vol%/mm Hg, the constant used in Eq. 5 in the resting studies (Table A-XI, col. 2), but increased with rising hemoglobin content to a mean value of .503 vol%/mm Hg. It was shown earlier that cardiac output calculated from arterial and mixed venous $P_{CO2}$ in the blood tended to overestimate as compared to the direct Fick calculation (Table A-V). This would not have been the case if the actual slope values had been used instead of a constant 4.7.

## IV. Summary and Conclusions

Estimates of cardiac output by the single-breath method of Kim, Rahn, and Farhi were compared with simultaneous determinations with the direct Fick procedure in 20 tests on 5 subjects during right heart catheterization. The two methods showed good correlation, but the single-breath method gave results that were systematically lower than the direct measurements. For future use of the SB method it is proposed to use the regression equation obtained in this study to estimate $\dot{Q}_F$ from $\dot{Q}_{SB}$ in order to minimize the systematic error.

$$\dot{Q}_{F'} = 1.28\,\dot{Q}_{SB} - 0.88 \qquad (4)$$

The SB records were re-examined and an improved procedure for point selection and curve-fitting (moving spline) applied. This further reduced the variance of the data. From these, a new regression was calculated to adjust for the systematic error:

$$\dot{Q}_{F'}^{sp} = 1.18\,\dot{Q}_{SB}^{sp} + .553 \qquad (11)$$

Using the new treatment on future SB determinations, there is a good chance that about 2/3 of the determinations will fall within 10% of the true value and less than 1/10 will be more than 20% in error.

The blood samples obtained in close proximity in time with the single-breath maneuver permitted a comparison of $P_{CO2}$ and R values from the expired gas and from direct analysis in the blood. Without exception, both mixed venous and arterial $P_{CO2}$'s were higher in the blood than in the gas

phase, but the difference was greater for the arterial values than the venous ones. Consequently, the slope of $P_{CO_2}$ vs R was greater for the SB data, which explains the underestimation of $\dot{Q}$ by the SB method. The assumption that the respiratory exchange ratio for blood ($R_B$) is equal to that in the mixed expired gas ($R_{\bar{E}}$) was found not to be true under resting conditions, where $R_B$ was consistently lower. However, $R_B$ was practically identical with $R_{\bar{E}}$ during submaximal exercise. The slope of the $CO_2$ combining curve calculated for blood on the basis of hemoglobin concentration was close to the value used by the originators of the SB method (4.7 ml/L/mm Hg) in their modified Fick equation. However, the actual values in the blood increased to 5.03 ml/L/mm Hg during the most strenuous exercise because hemoglobin concentration was higher. Finally, the constant used in the modified Fick equation for the Haldane effect was found to be considerably lower calculated from the blood gas data than the figure 0.32 proposed by the originators under resting conditions, but agreement was much better in the exercise tests. Of the discrepancies revealed in this study between certain assumptions underlying the SB method and direct measurements, the inequality of alveolar and blood $P_{CO_2}$ values is by far the most important. Fortunately, this discrepancy is apparently sufficiently consistent to justify a systematic correction using the proposed regression equation to estimate true cardiac output.

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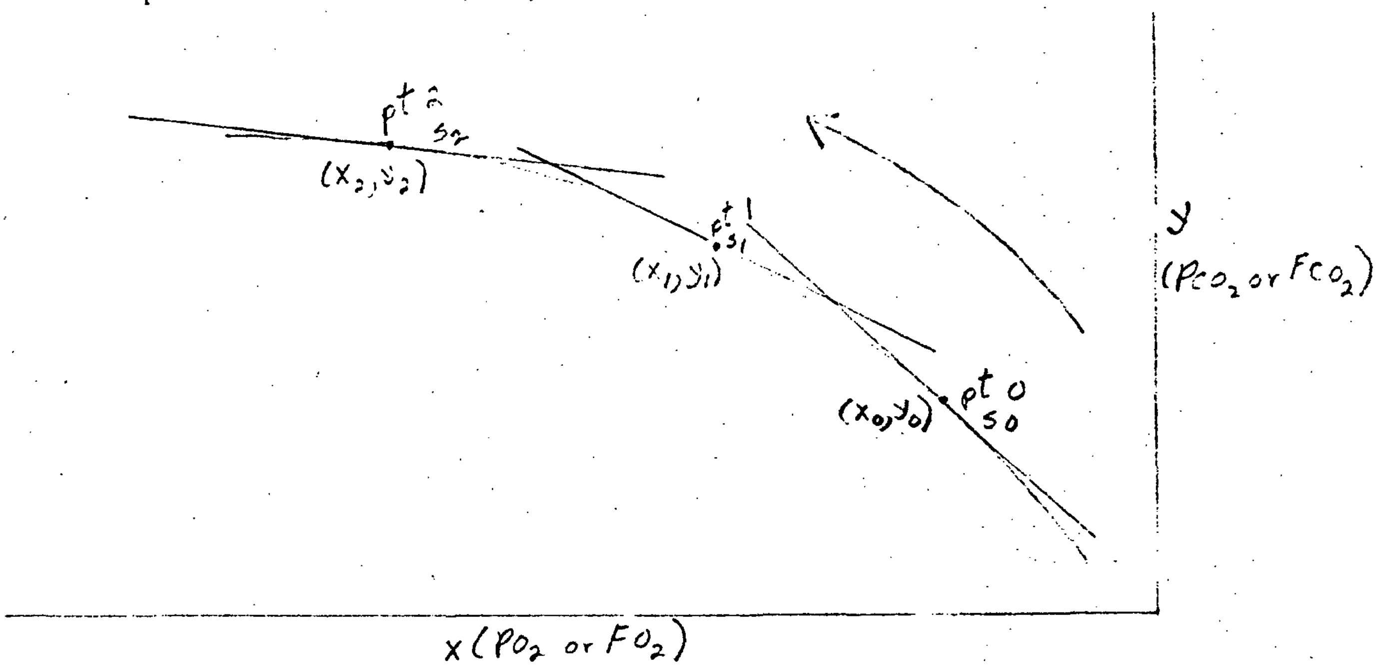
Derivation of equations and procedure for using a three-point "moving spline" technique to obtain the coordinates for the R vs $P_{CO_2}$ curve from the $X(P_{O_2}) - Y(P_{CO_2})$ curve.

Derivations:

It is assumed that the equation of the curve is a second degree polynomial, i.e.

$$y = A + Bx + Cx^2 \tag{V-1}$$

and that the constants in this equation are allowed to change while moving along the curve, considering three data points at a time, which are chosen equidistant on the X-axis.




The slope, S, of the curve may be obtained by differentiating Eq. 1 to give

$$S = B + 2Cx \tag{V-2}$$

For point (0)

$$y_o = A + Bx_o + Cx_o^2 \tag{V-3}$$

and

$$S_o = B + 2Cx_o \tag{V-4}$$

Rearranging Eq. 4 gives

$$B = S_o - 2Cx_o \tag{V-5}$$

Substituting Eq. 5 into Eq. 3 and rearranging gives

$$A = y_o - S_o x_o + C x_o^2 \tag{V-6}$$

Substituting Eqs. 5 and 6 into Eqs. 1 and 2 and rearranging gives

$$y = y_o + S_o(x-x_o) + C(x-x_o)^2 \tag{V-7}$$

and

$$S = S_o + 2C(x-x_o) \tag{V-8}$$

We want to determine C in such a way as to minimize the sum of the squares of the differences between the y's read from the curve and the y's computed from Eq. 7. This can be done by setting the partial derivitive of this sum with respect to C equal to zero.

$$\frac{\delta \sum_{i=1}^{2} \left[ y_i - y_o - S_o(x_i - x_o) - C(x_i - x_o)^2 \right]^2}{\delta C} = 0 \tag{V-9}$$

which gives

$$\sum_{i=1}^{2} (x_i - x_o)^2 \left[ y_i - y_o - S_o(x_i - x_o) - C(x_i - x_o)^2 \right] = 0 \tag{V-10}$$

or

$$\sum_{i=1}^{2} (x_i - x_o)^2 \left[ y_i - y_o - S_o(x_i - x_o) \right] = C \sum_{i=1}^{2} (x_i - x_o)^4 \tag{V-11}$$

and rearranging

$$C = \frac{\sum_{i=1}^{2} (x_i - x_o)^2 \left[ (y_i - y_o) - S_o(x_i - x_o) \right]}{\sum_{i=1}^{2} (x_i - x_o)^4} \tag{V-12}$$

or

$$C = \frac{(x_1 - x_o)^2 \left[ (y_1 - y_o) - S_o(x_1 - x_o) \right] + (x_2 - x_o)^2 \left[ (y_2 - y_o) - S_o(x_2 - x_o) \right]}{(x_1 - x_o)^4 + (x_2 - x_o)^4} \tag{V-13}$$

Equation 13 gives the value for C over points 0, 1, and 2 (although C is actually only used in computing the curve from points 0 and 1) if one knows the coordinates of the points and the slope at point 0. The constants B and A for the same interval can be computed from Eqs. 5 and 6.

$y_1$ can then be computed (the middle of the three points considered) by Eq. 14 and this value should be very close to the $y_1$ read from the curve.

$$y_1 \text{ computed} = A + Bx_1 + Cx_1^2 \tag{V-14}$$

$y_1$ can be computed from actual data points by eliminating A and B from Eq. 14, i.e., by substituting Eqs. 5 and 6 in Eq. 14.

$$y_1 \text{ computed} = y_o + S_o(x_1-x_o) + C(x_1-x_o)^2 \tag{V-15}$$

This is Eq. 7 for $x=x_1$.

$S_1$, the slope through the point $(x_1,y_1)$, can be obtained from Eq. 2 and this computed slope should be the tangent to the curve at that point, i.e.

$$S_1 \text{ computed} = B + 2Cx_1 \tag{V-16}$$

and by substituting Eq. 5 in 16

$$S_1 \text{ computed} = S_o + 2C(x_1-x_o) \tag{V-17}$$

This is Eq. 8 for $x=x_1$.

The equation of the tangent through ($x_1$, $y_1$ computed) can be obtained from Eq. 18.

$$y = y_1 \text{ computed} + S_1 \text{ computed } (x-x_1) \tag{V-18}$$

Procedure:

1) This method can be used when three or more points are chosen from the X-Y plot. We chose 11 points from each curve equidistant on the x-axis, starting at the upper end. If six points are chosen, five slopes will be obtained, four of these being computed.

2) A tangent is drawn by eye to the curve at point $(x_o, y_o)$. This is $S_o$. On the standard X-Y plot, $S_o$ is negative.

3) The remaining coordinates $(F_{O_2}, F_{CO_2})$ read from the X-Y curve for each of the points selected are tabulated. For convenience in arithmetic manipulations each of the coordinates can be multiplied by 100.

4) The constant, C, is calculated from Eq. 13 using the coordinates at points 0, 1, and 2 for $S_o$.

5) The value for $y_1$ is computed from Eq. 15. This value should be very close to the $y_1$ read from the curve.

6) The slope, $S_1$, is computed from Eq. 17. If desirable the tangent through the point $(x_1,y_1)$ can be drawn to visually determine if $S_1$ is a good estimate of the slope of the X-Y plot, i.e., by substituting any x into Eq. 18 and computing the corresponding value of y.

7) One is then ready to move along the curve and to obtain $S_2$ in a similar manner. The $y_1$ computed, becomes the new $y_o$ in Eq. 13 and $x_1$, $x_2$, and $x_3$ from the X-Y plot become $x_o$, $x_1$ and $x_2$ respectively, in the same equation, while $y_2$ and $y_3$ off the curve become $y_1$ and $y_2$ and $S_1$ computed becomes $S_o$.

The new calculated value for C is then the constant in the equation between the points originally numbered 1, 2, and 3 (although it will only be used to compute the curve between points 1 and 2).

8) The value for $y_2$ is then computed from Eq. 15 and $S_2$ from Eq. 17. The new slope at point $(x_2,y_2)$ can again be drawn in for visual comparison by the use of Eq. 18.

9) This process is continued until all points have been used.

10) The slopes and computed values for $y(F_{CO_2})$ and values read from the curve for $x(F_{O_2})$ are tabulated. The slopes can be converted to R values by Eq. I in Section II of this appendix, using the corresponding S computed, x, and y computed values for each point.

11) The computed $y(F_{CO2})$ values are converted to $P_{CO2}$ values and plotted against the corresponding values for R and a best fit straight line is calculated from which $P\bar{v}_{CO_2}$ and $Pa_{CO_2}$ can be estimated and $\dot{Q}$ calculated.

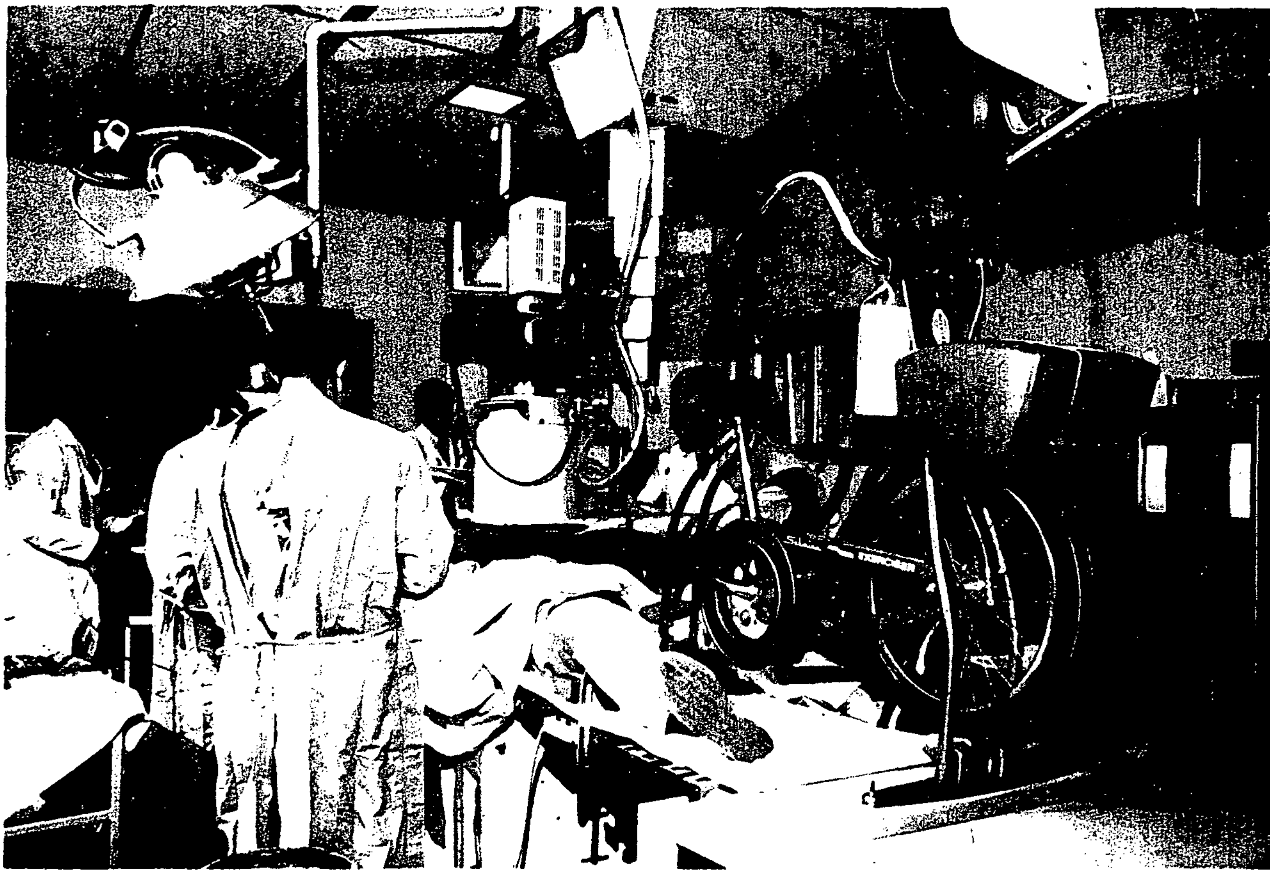


Fig. A-1. Measurement of cardiac output by the direct Fick and single-breath methods in the Cardiac Catheterization Laboratory of the Lovelace-Bataan Medical Center

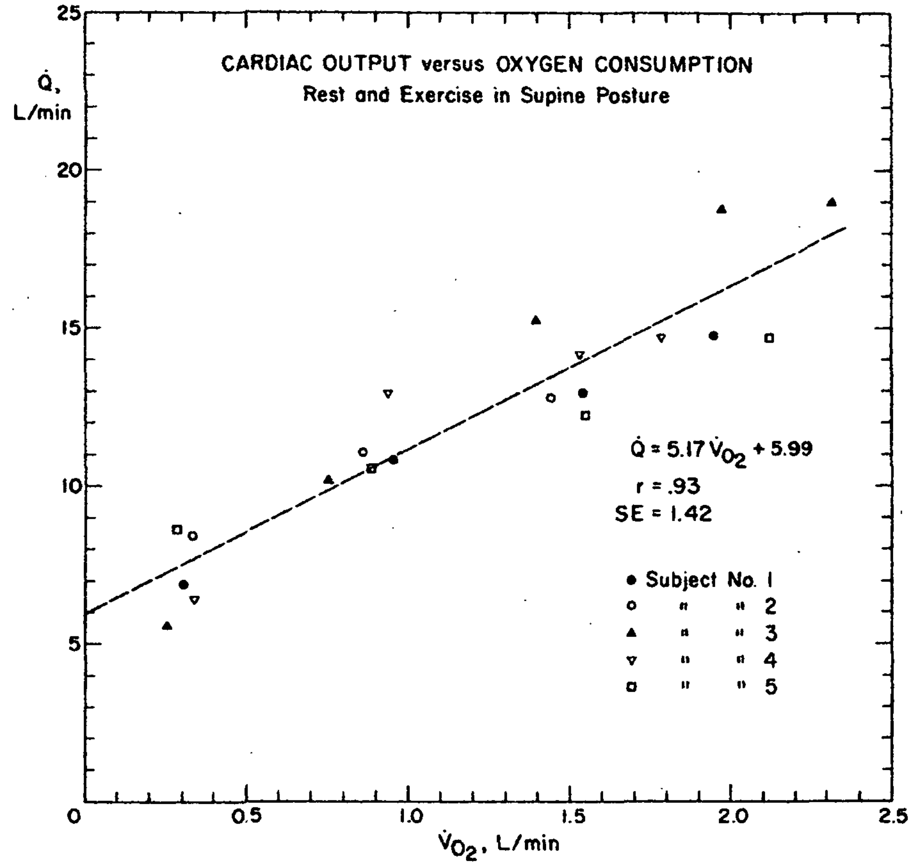



**Fig. A-2.** Cardiac output by the Fick method as a function of metabolic rate (supine posture)

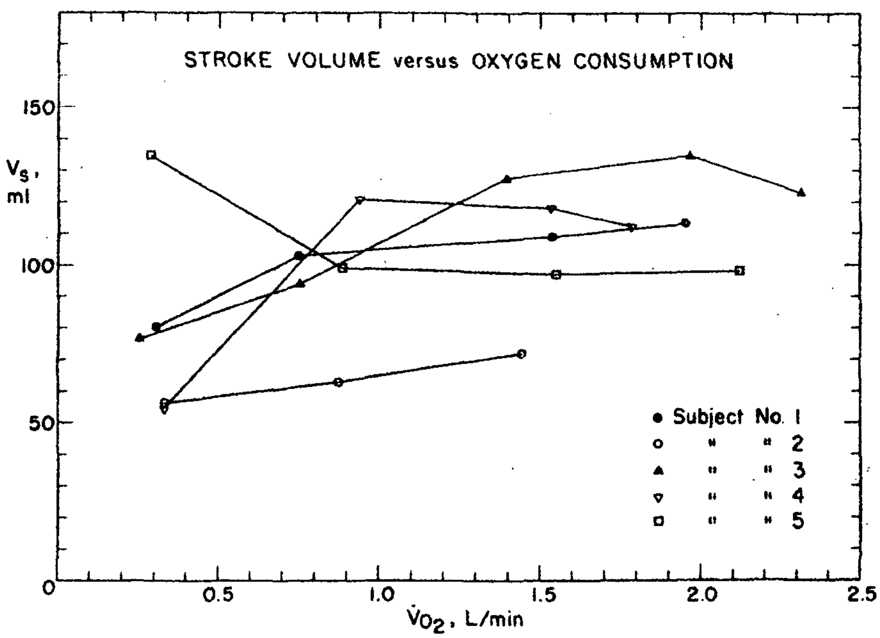



Fig. A-3. Stroke volume as a function of metabolic rate (supine posture)

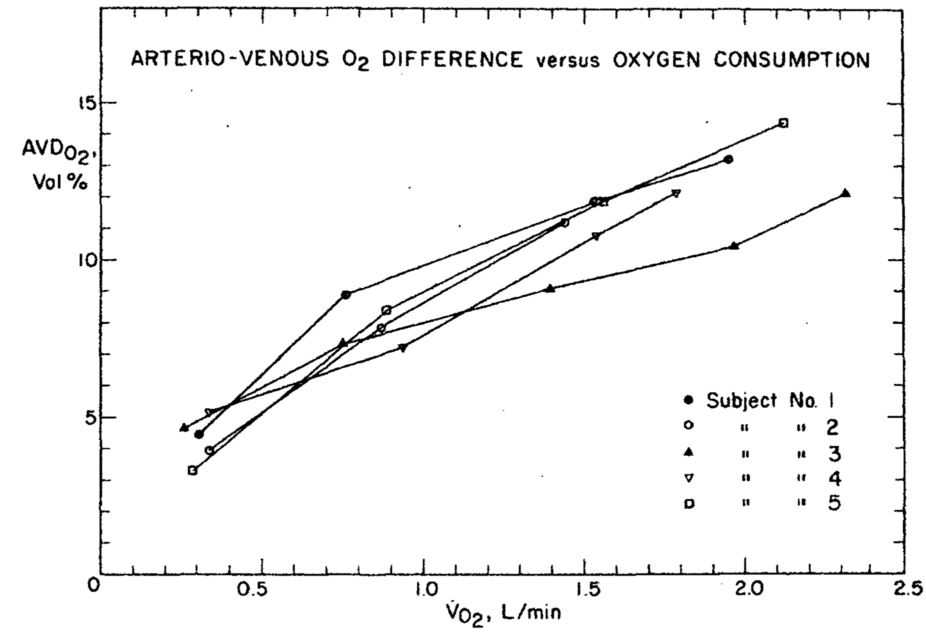



Fig. A-4. Arterio-mixed venous difference for oxygen as a function of metabolic rate (supine posture)

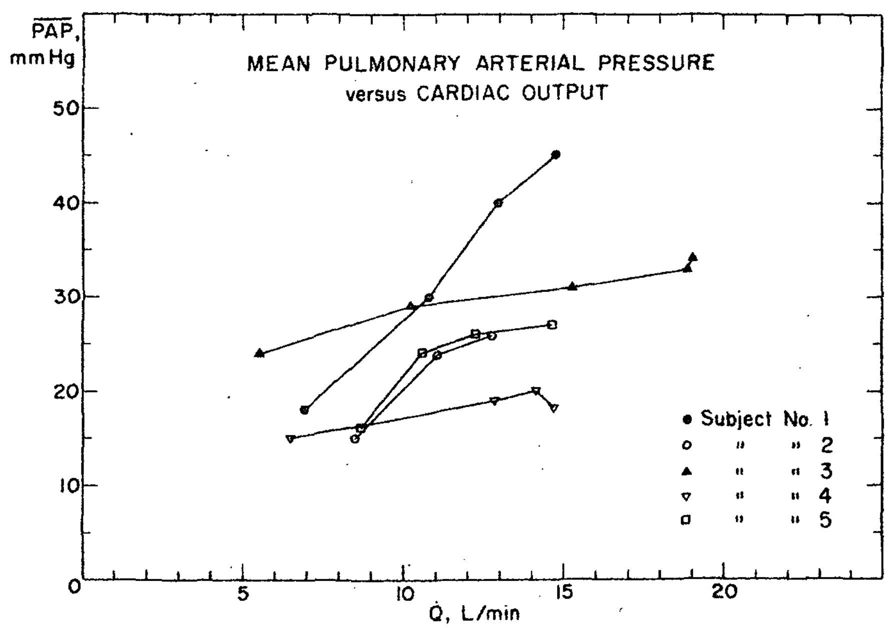



Fig. A-5. Mean pulmonary arterial pressure as a function of cardiac output

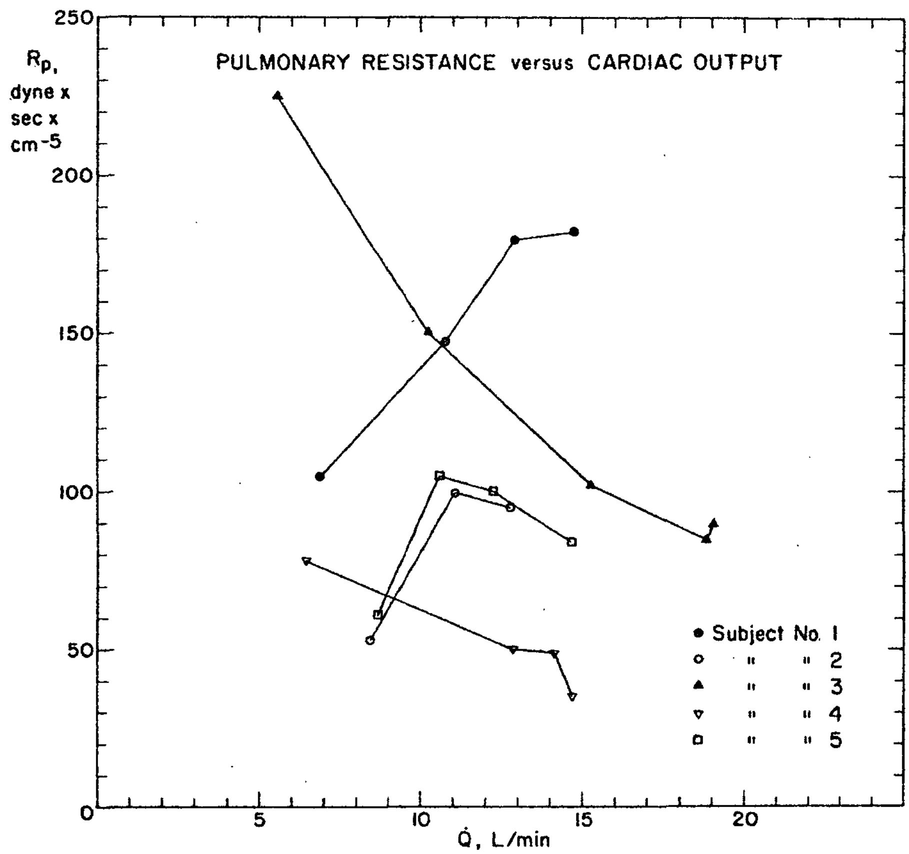



Fig. A-6. Pulmonary vascular resistance versus cardiac output at rest and supine exercise

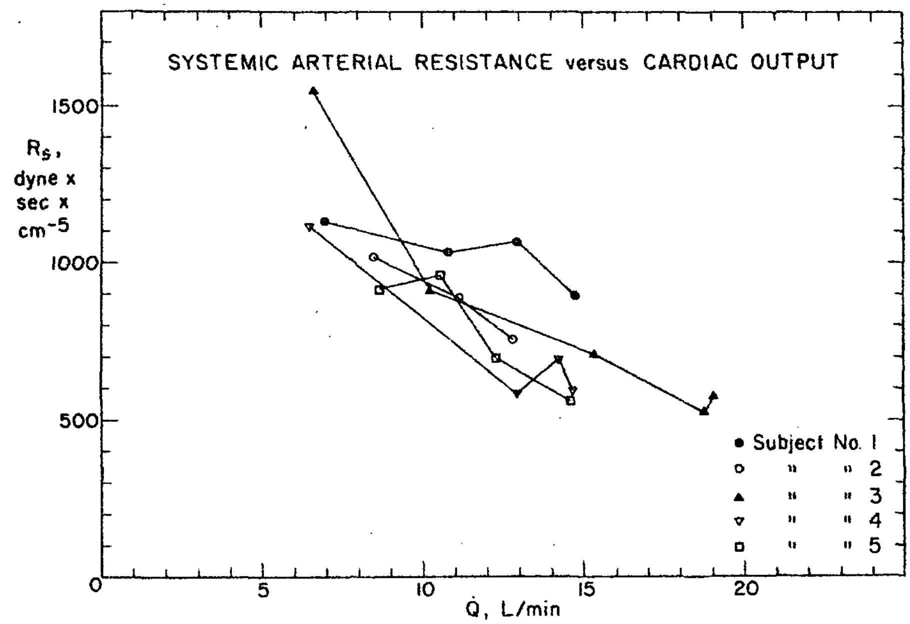



Fig. A-7. Systemic vascular resistance versus cardiac output at rest and during supine exercise

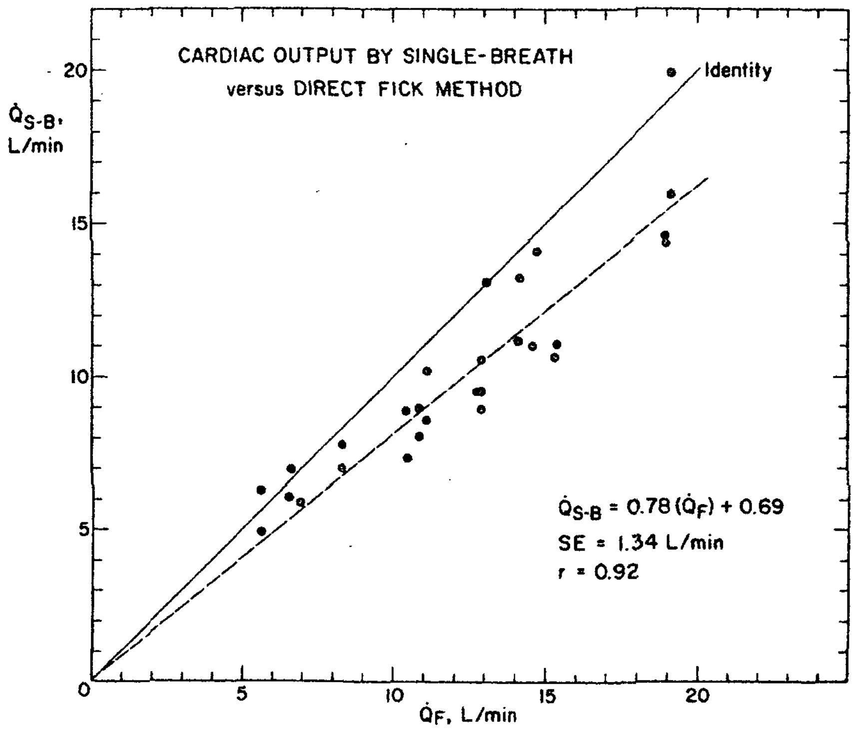



Fig. A-8. Cardiac output by the single-breath method ($\dot{Q}_{SB}$) versus the direct Fick method ($\dot{Q}_F$)

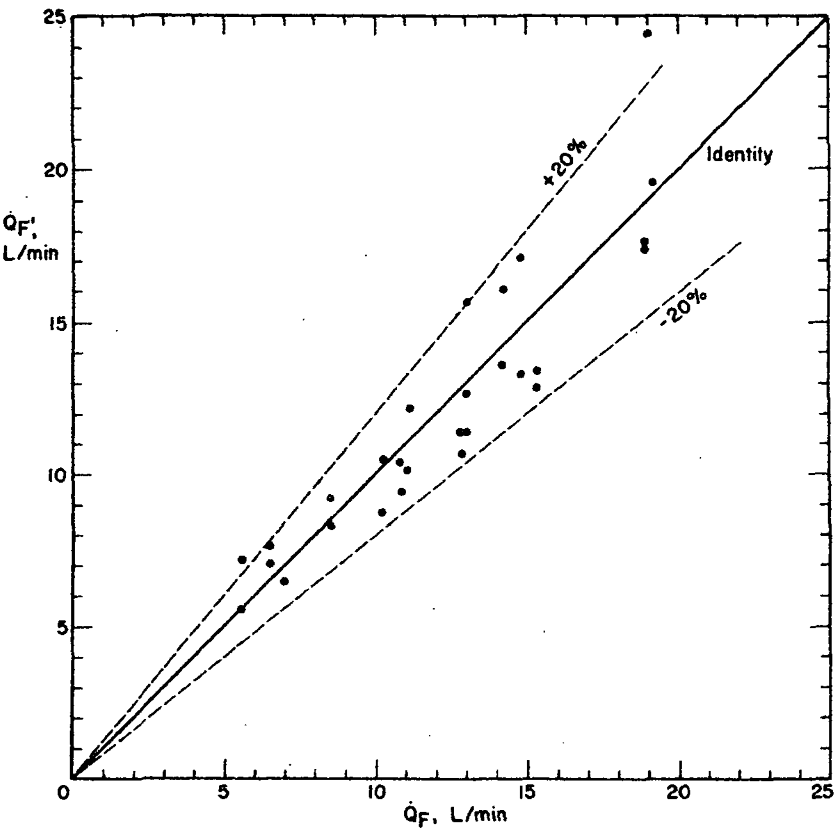



Fig. A-9. Cardiac output predicted from the single-breath measurements, but corrected with regression Eq. 4, $\dot{Q}_{F'}$ compared with the direct Fick method ($\dot{Q}_F$)

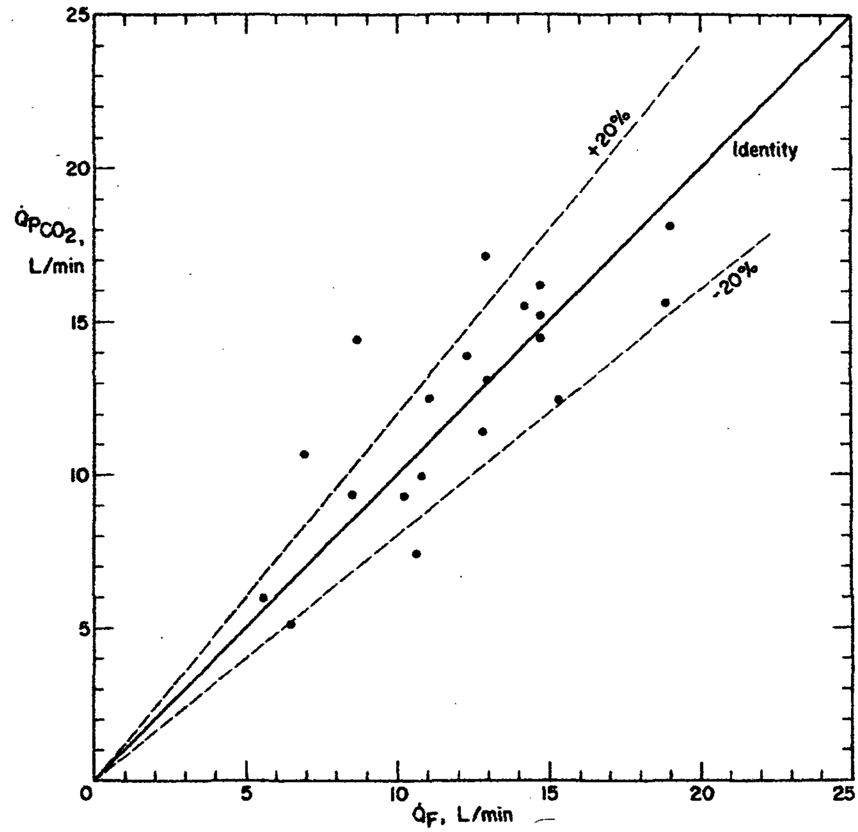



Fig. A-10. Cardiac output calculated from direct measurements of arterial and mixed venous $P_{CO2}$ with the modified Fick equation (5) versus the direct Fick method

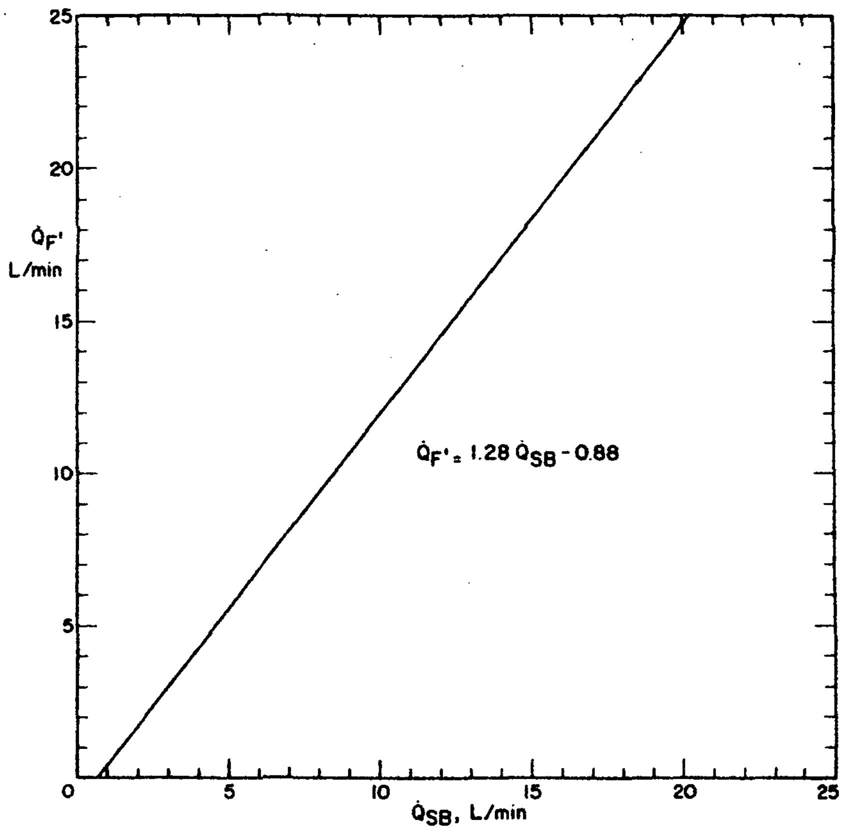



Fig. A-11. Regression line for estimating true cardiac output ($\dot{Q}_{F'}$) from the single-breath method ($\dot{Q}_{SB}$)

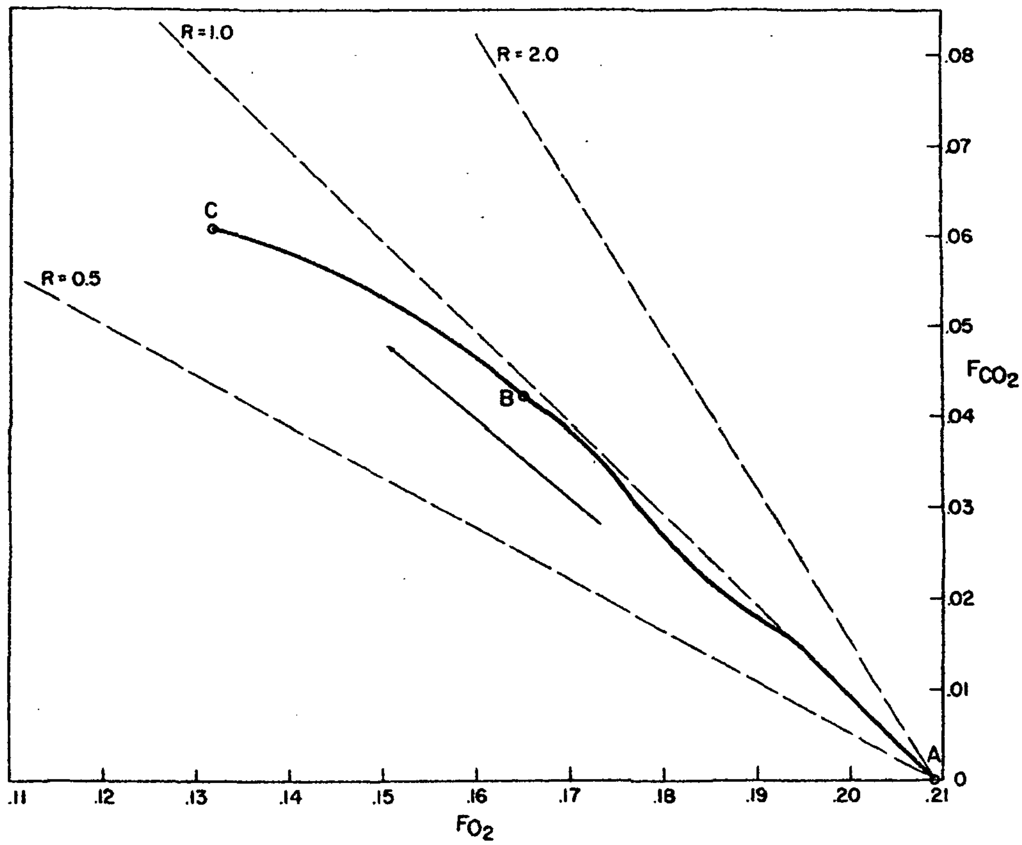



Fig. A-12. Example of a single prolonged expiration plotted on the $O_2$-$CO_2$ diagram with an X-Y recorder

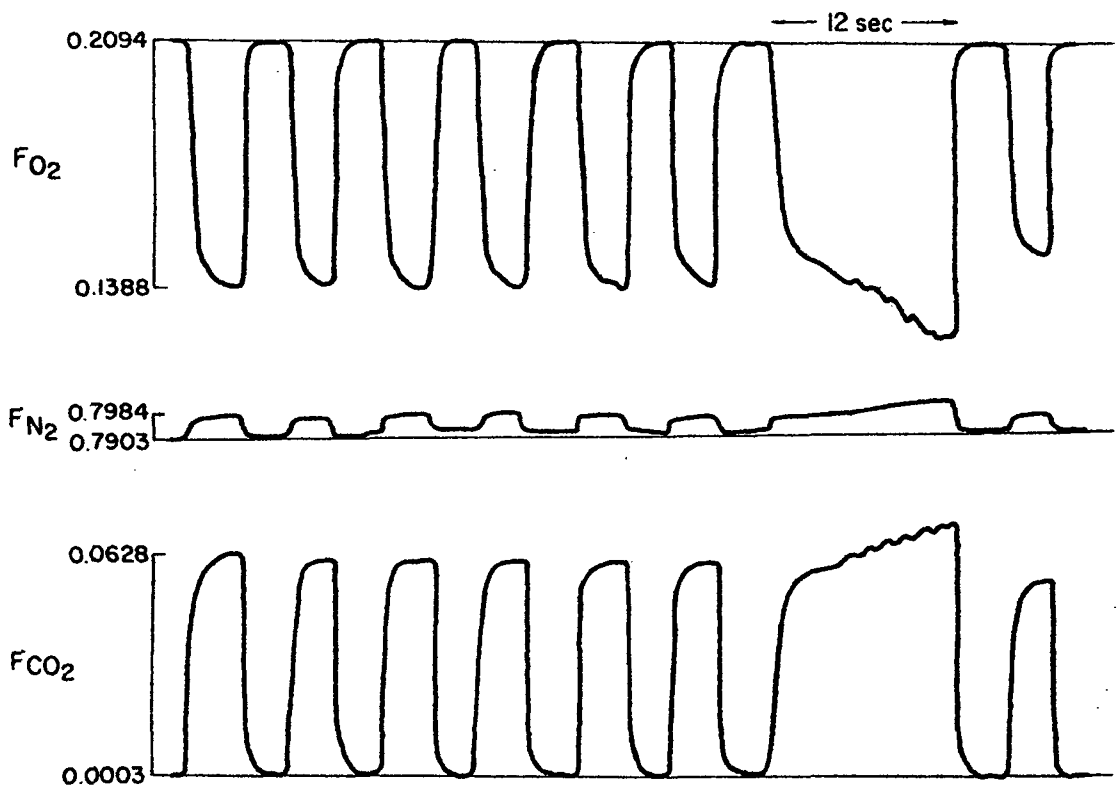



Fig. A-13. Example of a single prolonged breath on the oscillograph recorder

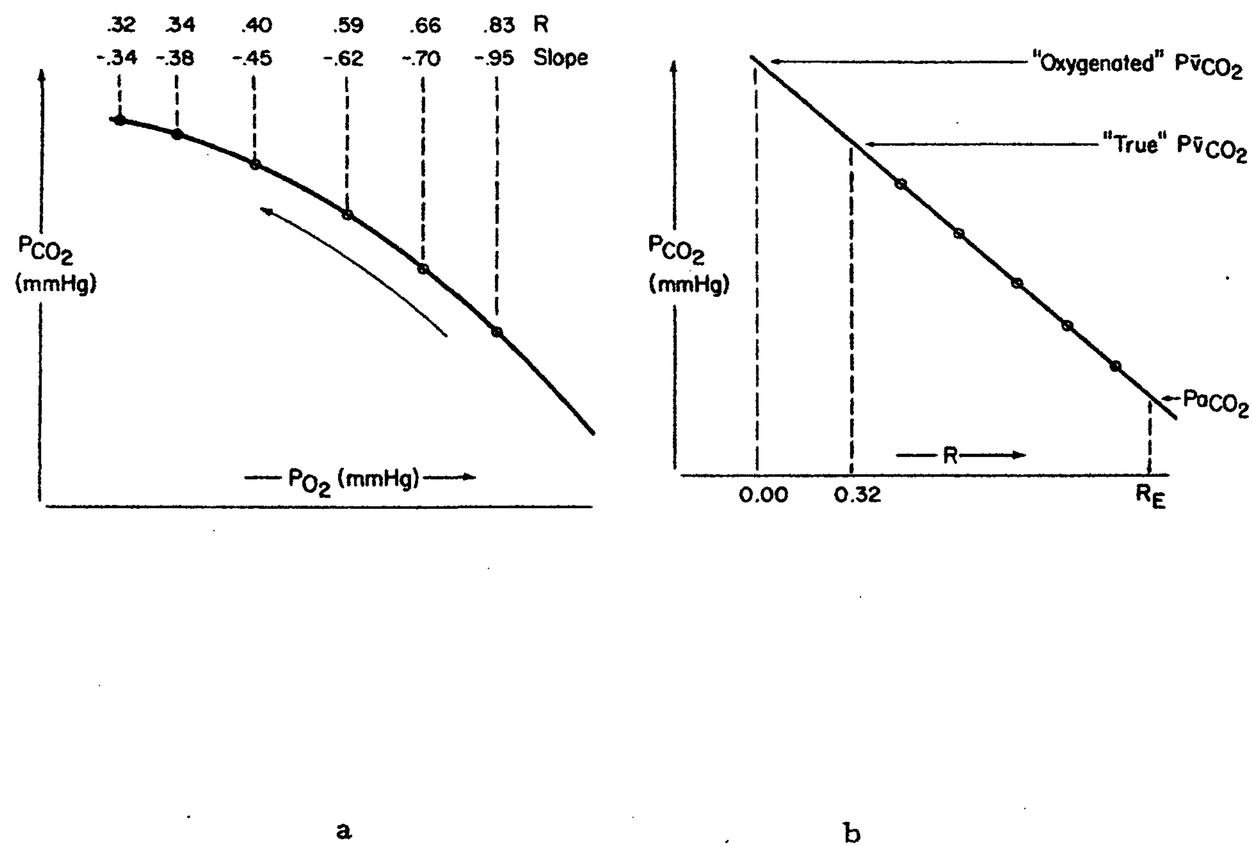



Fig. A-14a. Selection of points on the SB curve to determine slope and R values [according to Kim, et. al. (6)]

Fig. A-14b. The $P_{CO_2}$ versus R values obtained from the record above

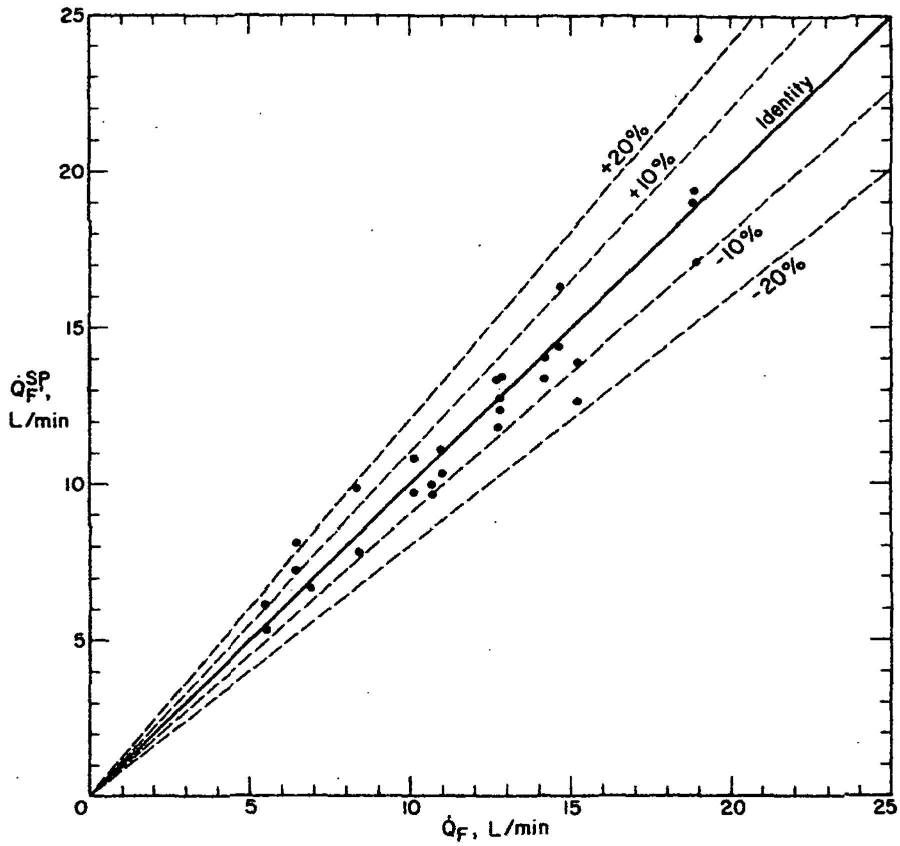



Fig. A-15. Cardiac output from a single breath with curve-fitting by the moving spline method and corrected for systematic error by Eq. 11, compared with direct Fick determinations

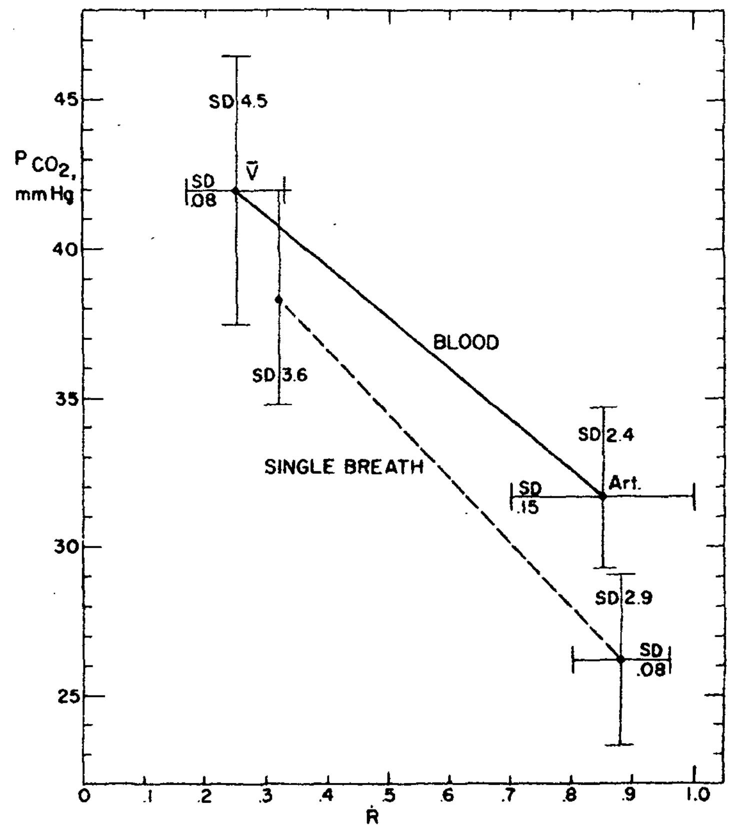



Fig. A-16. Arterial and mixed venous points on the $P_{CO_2}$-R line from the mean values of all SB records and from simultaneous blood samples with one standard deviation

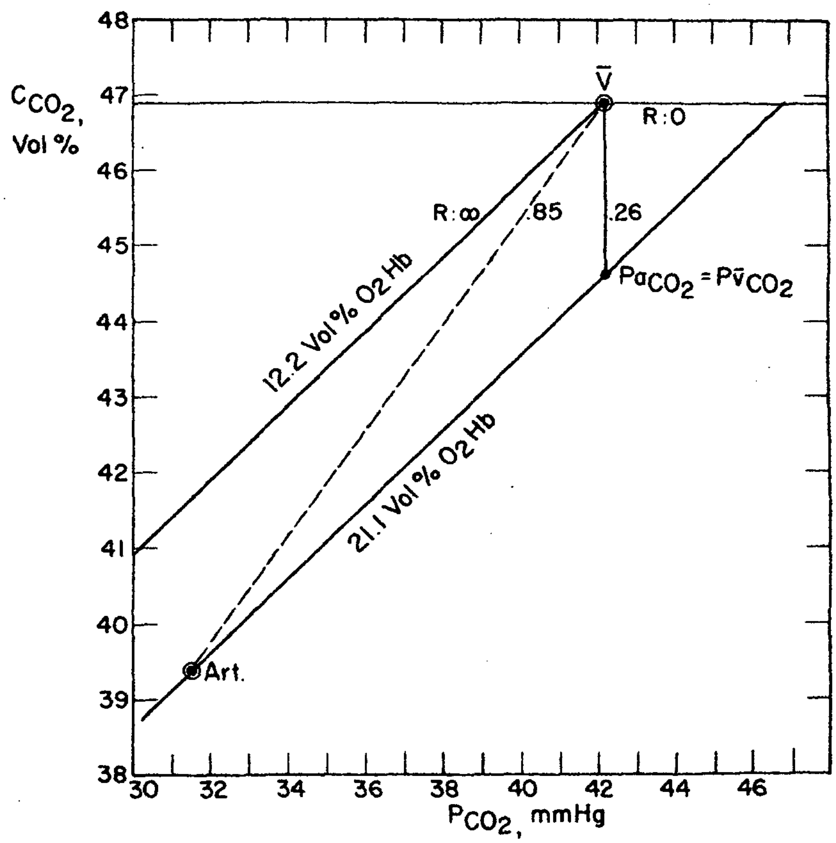



Fig. A-17. $CO_2$ combining curve for arterial and mixed venous blood (mean values at rest and exercise from 20 tests). The difference in $CO_2$ content at the mixed venous point ($\bar{v}$) and the point where $Pa_{CO_2} = P\bar{v}_{CO_2}$ is the amount of $CO_2$ removed by the Haldane effect and gives $R_H$ (see text)

Table A-I

Physical and Functional Characteristics of the Subjects

| Subject | #1 LU | #2 AT | #3 MY | #4 CO | #5 DE |
|---|---|---|---|---|---|
| Age | 62 | 34 | 35 | 30 | 43 |
| Height - cm | 180 | 183.5 | 187.5 | 185 | 179 |
| Weight - kg | 81.0 | 84.0 | 80.0 | 96.0 | 80.0 |
| BSA - $m^2$ | 2.00 | 2.06 | 2.07 | 2.21 | 2.00 |
| Total Lung Capacity - L | 7.74 | 8.51 | 7.77 | 7.79 | 7.35 |
| Vital Capacity - L | 5.24 | 6.67 | 6.43 | 6.76 | 5.71 |
| Max Mid-expiratory Flow - L/sec | 2.33 | 3.63 | 4.36 | 8.50 | 2.33 |
| Nitrogen Clearance Equiv. | 15.0 | 9.2 | 9.4 | 10.7 | 9.5 |
| Diffusing Capacity (CO) - ml/mm Hg/min | 25.0 | 43.7 | 47.6 | 38.0 | 20.0 |
| Max $O_2$ Intake - L/min | 2.971 | 3.578 | 4.411 | 3.565 | 2.918 |
| Max $O_2$ Intake per kg | 36.7 | 42.6 | 55.1 | 37.0 | 36.5 |
| Max Heart Rate (exercise) | 168 | 180 | 191 | 188 | 181 |

Table A-II CARDIOVASCULAR FUNCTIONS

| Subj. Age | Work kgm/min | $\dot{V}_{O_2}$ L/min | $AVD_{O_2}$ Vol% | $\dot{Q}$ L/Min | HR per min | $V_s$ ml | PAP mmHg | $\overline{PAP}$ mmHg | $R_p$ dyne x sec x $cm^{-5}$ | SAP mmHg | $\overline{SAP}$ mmHg | Rs dyne x sec x $cm^{-5}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LU 62y | 0 | .305 | 4.40 | 6.93 | 87 | 80 | 25/14 | 18 | 105 | 141/71 | 101 | 1131 |
| | 300 | .957 | 8.86 | 10.80 | 105 | 103 | 41/17 | 30 | 147 | 167/128 | 142 | 1030 |
| | 600 | 1.538 | 11.87 | 12.96 | 119 | 109 | 50/27 | 40 | 180 | 258/122 | 177 | 1074 |
| | 750 | 1.949 | 13.23 | 14.73 | 130 | 113 | 55/32 | 45 | 182 | 246/113 | 167 | 891 |
| AT 34y | 0 | .331 | 3.91 | 8.47 | 150+ | 56 | 28/4 | 15 | 53 | 142/96 | 111 | 1020 |
| | 300 | .864 | 7.83 | 11.03 | 174+ | 63 | 37/14 | 24 | 100 | 158/106 | 126 | 892 |
| | 600 | 1.443 | 11.27 | 12.80 | 179+ | 72 | 40/16 | 26 | 95 | 148/97 | 124 | 756 |
| MY 36y | 0 | .257 | 4.64 | 5.54 | 72 | 77 | 36/13 | 24 | 225 | 152/82 | 110 | 1545 |
| | 300 | .752 | 7.37 | 10.20 | 108 | 94 | 35/21 | 29 | 150 | 107/88 | 119 | 910 |
| | 600 | 1.395 | 9.13 | 15.28 | 119 | 128 | 43/15 | 31 | 102 | 208/101 | 139 | 712 |
| | 900 | 1.965 | 10.42 | 18.86 | 140 | 135 | 56/16 | 33 | 85 | 211/93 | 127 | 528 |
| | 1050 | 2.316 | 12.17 | 19.03 | 155 | 123 | 61/13 | 34 | 84 | 227/102 | 140 | 576 |
| CO 30y | 0 | .331 | 5.10 | 6.49 | 119+ | 55 | 25/3 | 15 | 78 | 127/83 | 98 | 1171 |
| | 300 | .932 | 7.20 | 12.94 | 107 | 121 | 35/2 | 19 | 50 | 126/81 | 97 | 581 |
| | 600 | 1.530 | 10.79 | 14.18 | 120 | 118 | 34/2 | 20 | 49 | 166/101 | 126 | 694 |
| | 750 | 1.785 | 12.13 | 14.72 | 131 | 112 | 28/7 | 18 | 35 | 161/90 | 133 | 598 |
| DE 44y | 0 | .282 | 3.26 | 8.65 | 64 | 135 | 30/9 | 16 | 61 | 138/75 | 102 | 916 |
| | 300 | .882 | 8.34 | 10.56 | 107 | 99 | 38/16 | 24 | 105 | 166/105 | 129 | 958 |
| | 600 | 1.546 | 11.88 | 13.01 | 127 | 97 | 42/14 | 26 | 109 | 129/91 | 110 | 698 |
| | 750 | 2.116 | 14.41 | 14.68 | 150 | 98 | 37/18 | 27 | 84 | 134/86 | 106 | 561 |

Key:

$\dot{V}_{O_2}$ : oxygen intake

$AVD_{O_2}$ : arterio-venous $O_2$ difference

$\dot{Q}$ : cardiac output

HR : Heart Rate

Vs : Stroke volume

PAP : Pulmonary arterial Pressure

$\overline{PAP}$ : Mean PAP

$R_p$ : Pulmonary vascular resistance

SAP : Systemic arterial pressure

$\overline{SAP}$ : Mean SAP

Rs: Systemic vascular resistance

+) atrial fibrillation

Table A-III ALVEOLAR AND BLOOD GASES

| Subject Work kpm/min | $P_{A O_2}$ mmHg | $P_{a O_2}$ mmHg | $P_A - a_{O_2}$ mmHg | $S_{a O_2}$ % | $P_{\bar{v} O_2}$ mmHg | $S_{\bar{v} O_2}$ % | $Cap_{O_2}$ Vol % | $P_aCO_2$ mmHg | $P_ACO_2$ mmHg | $P_a$-A $CO_2$ mmHg | pHa | $BE_a$ mEq/L | $P_{\bar{v}}CO_2$ mmHg | $pH_{\bar{v}}$ | $BE_{\bar{v}}$ mEq |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LU 0 | 88.5 | 62.3 | 26.2 | 94% | 37.8 | 74% | 22.4 | 28.6 | 27.3 | 1.3 | 7.51 | 1.2 | 31.4 | 7.49 | 2.0 |
| 300 | 84.5 | 60.7 | 23.8 | 93% | 27.8 | 54% | 24.5 | 31.0 | 30.9 | 0.1 | 7.47 | .2 | 38.6 | 7.42 | .8 |
| 600 | 89.5 | 63.9 | 25.6 | 93% | 24.2 | 41% | 25.0 | 27.3 | 30.0 | -2.7 | 7.43 | -4.2 | 42.1 | 7.35 | -2.3 |
| 750 | 90.8 | 60.7 | 30.1 | 92% | 22.2 | 33% | 25.8 | 26.4 | 29.3 | -2.9 | 7.41 | -6.0 | 43.0 | 7.32 | -3.9 |
| AT 0 | 89.0 | 80.8 | 8.2 | 97% | 42.7 | 81% | 21.9 | 29.8 | 29.0 | 0.8 | 7.50 | 1.5 | 33.8 | 7.47 | 1.8 |
| 300 | 81.9 | 73.2 | 8.7 | 96% | 32.1 | 64% | 23.8 | 31.7 | 33.2 | -1.5 | 7.46 | -0.3 | 38.6 | 7.42 | -0.5 |
| 600 | 90.4 | 79.2 | 11.2 | 96% | 26.0 | 45% | 24.8 | 31.1 | 32.4 | -1.3 | 7.43 | -2.0 | 45.2 | 7.35 | -0.9 |
| MY 0 | 81.8 | 76.5 | 5.3 | 96% | 40.4 | 77% | 21.4 | 34.8 | 36.9 | -2.1 | 7.47 | 2.7 | 40.4 | 7.44 | 2.5 |
| 300 | 73.4 | 64.0 | 9.4 | 94% | 28.8 | 57% | 22.0 | 34.0 | 40.8 | -6.8 | 7.47 | 2.0 | 42.3 | 7.41 | 2.1 |
| 600 | 72.8 | 61.2 | 11.6 | 93% | 25.7 | 47% | 22.4 | 36.1 | 42.6 | -6.5 | 7.45 | 1.3 | 48.3 | 7.38 | 2.7 |
| 900 | 82.1 | 67.6 | 14.5 | 94% | 25.1 | 43% | 22.9 | 32.6 | 37.6 | -5.0 | 7.44 | -1.1 | 48.7 | 7.35 | 0.5 |
| 1050 | 86.3 | 68.6 | 17.7 | 94% | 22.8 | 36% | 23.0 | 30.2 | 34.3 | -4.1 | 7.44 | -2.4 | 47.1 | 7.35 | -0.8 |
| CO 0 | 87.5 | 74.3 | 13.2 | 96% | 38.4 | 75% | 22.9 | 31.1 | 30.6 | 0.5 | 7.49 | 1.2 | 38.7 | 7.45 | 2.9 |
| 300 | 84.7 | 65.1 | 19.3 | 94% | 30.8 | 62% | 24.3 | 33.9 | 31.8 | 2.1 | 7.47 | 1.5 | 39.8 | 7.42 | 1.8 |
| 600 | 88.3 | 67.0 | 21.3 | 94% | 25.0 | 46% | 24.9 | 31.8 | 30.1 | 1.7 | 7.46 | -0.1 | 43.6 | 7.39 | 1.0 |
| 750 | 90.2 | 71.5 | 18.7 | 95% | 23.2 | 40% | 24.2 | 30.0 | 28.9 | 1.1 | 7.47 | -0.4 | 43.6 | 7.38 | 0.5 |
| DE 0 | 92.1 | 61.8 | 30.3 | 93% | 40.0 | 78% | 21.9 | 32.3 | 27.7 | 4.6 | 7.47 | 1.1 | 34.8 | 7.46 | 1.9 |
| 300 | 76.3 | 65.2 | 11.1 | 94% | 27.8 | 52% | 22.3 | 33.5 | 35.1 | -1.6 | 7.44 | -0.3 | 43.9 | 7.40 | 2.1 |
| 600 | 87.4 | 72.8 | 14.6 | 95% | 25.8 | 42% | 23.3 | 33.7 | 33.7 | 0 | 7.39 | -3.3 | 49.6 | 7.31 | -2.3 |
| 750 | 95.1 | 81.0 | 14.1 | 96% | 23.4 | 33% | 24.5 | . | 27.8 | -1.3 | 7.37 | -8.7 | 49.5 | 7.25 | -6.7 |

$P_{A O_2}$: Alveolar $P_{O_2}$

$P_{a O_2}$: arterial $P_{O_2}$

$S_{a O_2}$: arterial $O_2$ Sat.

$P_{\bar{v} O_2}$: mixed venous $P_{O_2}$

$S_{\bar{v}} O_2$: mixed venous $O_2$ Sat.

$CapO_2$: oxygen capacity

$P_aCO_2$: arterial $PCO_2$

$P_ACO_2$: alveolar $PCO_2$

$pH_a$: arterial pH

$BE_a$: arterial Base Excess

$pH_{\bar{v}}$: Mixed venous pH

$BE_{\bar{v}}$ : Mixed venous base-excess

Table A-IV RESPIRATORY GAS EXCHANGE AND VENTILATION

| Subject | Work kpm/min | $\dot{V}_{O_2}$ L/Min | $\dot{V}CO_2$ L/Min | RER | $\dot{V}_I$ L/Min | freq. | Vt L | $\dot{V}_a$ L/Min | $\dot{V}a/\dot{V}_I$ | $\dot{V}_I/\dot{V}_{O_2}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| LU | 0 | .305 | .239 | .78 | 10.34 | 8 | 1.29 | 7.21 | .70 | 33.90 |
| | 300 | .957 | .756 | .79 | 28.06 | 16 | 1.75 | 21.05 | .75 | 29.30 |
| | 600 | 1.538 | 1.405 | .91 | 54.47 | 22 | 2.48 | 44.41 | .82 | 35.42 |
| | 750 | 1.949 | 1.809 | .93 | 73.13 | 24 | 3.05 | 59.14 | .81 | 37.52 |
| AT | 0 | .331 | .281 | .85 | 10.69 | 9 | 1.19 | 8.14 | .76 | 32.3 |
| | 300 | .864 | .680 | .79 | 21.62 | 13 | 1.66 | 18.51 | .86 | 25.0 |
| | 600 | 1.443 | 1.482 | 1.03 | 48.93 | 23 | 2.13 | 41.12 | .84 | 33.9 |
| MY | 0 | .257 | .229 | .89 | 6.34 | 3 | 2.11 | 5.68 | .90 | 24.67 |
| | 300 | .752 | .602 | .80 | 17.16 | 5 | 3.43 | 15.28 | .89 | 22.82 |
| | 600 | 1.395 | 1.161 | .83 | 30.87 | 9 | 3.43 | 27.75 | .90 | 22.13 |
| | 900 | 1.965 | 1.806 | .92 | 54.47 | 17 | 3.20 | 47.81 | .88 | 27.72 |
| | 1050 | 2.316 | 2.172 | .94 | 68.36 | 23 | 2.97 | 62.07 | .91 | 29.52 |
| CO | 0 | .331 | .288 | .87 | 11.53 | 18 | .640 | 7.99 | .69 | 34.83 |
| | 300 | .932 | .774 | .83 | 30.56 | 38 | .800 | 19.70 | .64 | 32.79 |
| | 600 | 1.530 | 1.354 | .88 | 51.14 | 47 | 1.09 | 36.75 | .72 | 33.42 |
| | 750 | 1.785 | 1.605 | .90 | 65.03 | 52 | 1.25 | 46.17 | .71 | 36.43 |
| DE | 0 | .282 | .260 | .92 | 11.48 | 19 | .600 | 6.95 | .61 | 40.71 |
| | 300 | .882 | .645 | .73 | 20.77 | 17 | 1.220 | 16.62 | .80 | 23.55 |
| | 600 | 1.546 | 1.516 | .98 | 48.38 | 20 | 2.420 | 38.82 | .80 | 31.29 |
| | 750 | 2.115 | 2.244 | 1.06 | 88.60 | 30 | 2.950 | 73.08 | .82 | 41.89 |

$\dot{V}_{O_2}$: $O_2$ intake

$\dot{V}CO_2$: $CO_2$ output

RER: Respiratory Exchange Ratio

$\dot{V}_I$: Ventilation Inspired

$V_t$: Tidal Volume

$\dot{V}_a$: Effective Alveolar Ventilation

Table A-V

| | $\dot{V}_{O2}$ L/min | $\dot{Q}_F$ L/min | $\dot{Q}_{SB}$ L/min | $\dot{Q}_{F'}$ L/min |
|---|---|---|---|---|
| 1. | 0.305 | 6.93 | 5.77 | 6.51 |
| 2. | 0.957 | 10.80 | 8.08 | 9.47 |
| 3. | 0.957 | 10.80 | 8.86 | 10.47 |
| 4. | 1.538 | 12.96 | 12.94 | 15.71 |
| 5. | 0.331 | 8.47 | 7.14 | 8.33 |
| 6. | 0.331 | 8.47 | 7.87 | 9.21 |
| 7. | 0.864 | 11.03 | 8.62 | 10.17 |
| 8. | 0.864 | 11.03 | 10.23 | 12.23 |
| 9. | 1.443 | 12.80 | 9.64 | 11.47 |
| 10. | 1.443 | 12.80 | 9.07 | 10.74 |
| 11. | 0.257 | 5.54 | 4.98 | 5.50 |
| 12. | 0.257 | 5.54 | 6.32 | 7.22 |
| 13. | 0.752 | 10.20 | 8.88 | 10.50 |
| 14. | 0.752 | 10.20 | 7.42 | 8.63 |
| 15. | 1.395 | 15.28 | 11.16 | 13.42 |
| 16. | 1.395 | 15.28 | 10.80 | 12.96 |
| 17. | 1.965 | 18.86 | 14.47 | 17.67 |
| 18. | 1.965 | 18.86 | 14.40 | 17.58 |
| 19. | 2.316 | 19.03 | 19.87 | 24.59 |
| 20. | 2.316 | 19.03 | 16.02 | 19.65 |
| 21. | 0.331 | 6.49 | 6.65 | 7.64 |
| 22. | 0.331 | 6.49 | 6.18 | 7.04 |
| 23. | 0.932 | 12.94 | 9.65 | 11.49 |
| 24. | 0.932 | 12.94 | 10.62 | 12.73 |
| 25. | 1.530 | 14.18 | 11.30 | 13.60 |
| 26. | 1.530 | 14.18 | 13.27 | 16.13 |
| 27. | 1.785 | 14.72 | 11.07 | 13.31 |
| 28. | 1.785 | 14.72 | 14.09 | 17.18 |
| Mean | 1.127 | 12.16 | 10.19 | 12.18 |

| | $\dot{V}_{O2}$ L/min | $\dot{Q}_F$ L/min | $\dot{Q}_{PCO2}$ L/min |
|---|---|---|---|
| 1. | 0.305 | 6.93 | 10.66 |
| 2. | 0.957 | 10.80 | 12.60 |
| 3. | 1.538 | 12.96 | 13.05 |
| 4. | 1.949 | 14.73 | 15.24 |
| 5. | 0.331 | 8.47 | 9.33 |
| 6. | 0.864 | 11.03 | 12.52 |
| 7. | 1.443 | 12.80 | 11.35 |
| 8. | 0.257 | 5.54 | 5.99 |
| 9. | 0.752 | 10.20 | 9.25 |
| 10. | 1.395 | 15.28 | 12.41 |
| 11. | 1.965 | 18.86 | 15.58 |
| 12. | 2.316 | 19.03 | 18.08 |
| 13. | 0.331 | 6.49 | 5.10 |
| 14. | 0.932 | 12.94 | 17.14 |
| 15. | 1.530 | 14.18 | 15.45 |
| 16. | 1.785 | 14.72 | 16.20 |
| 17. | 0.282 | 8.65 | 14.40 |
| 18. | 0.882 | 10.56 | 7.40 |
| 19. | 1.546 | 13.01 | 13.66 |
| 20. | 2.116 | 14.68 | 14.48 |
| Mean | 1.174 | 12.09 | 12.49 |

Left: $O_2$ consumption ($\dot{V}_{O2}$), cardiac output by the direct Fick method ($\dot{Q}_F$), the single-breath method ($\dot{Q}_{SB}$), and $\dot{Q}_{F'}$ predicted from $\dot{Q}_{SB}$ by the equation $\dot{Q}_{F'} = 1.28\,\dot{Q}_{SB} - .88$.

Note: With two exceptions, $\dot{Q}_{SB}$ was measured before and after each $\dot{Q}_F$.

Right: $\dot{V}_{O2}$, $\dot{Q}_F$, and $\dot{Q}$ calculated from direct measurements of $P\bar{v}_{CO2}$ and $Pa_{CO2}$ in blood.

Table A-VI

| Method | n | $\bar{\Delta}$ L/min | $\bar{\Delta}$% | SD$\Delta$% | p | Distribution $>\dot{Q}_F$ | $<\dot{Q}_F$ | Range $<10\%$ | 10-20% | $>20\%$ |
|---|---|---|---|---|---|---|---|---|---|---|
| $\dot{Q}_{SB}$ | 28 | -1.97 | -15% | 12% | <.001 | 3 | 25 | 8 | 9 | 11 |
| $\dot{Q}_{F'}$ | 28 | + .02 | <1% | 14% | NS | 11 | 17 | 13 | 12 | 3 |
| $\dot{Q}_{PCO2}$ | 20 | + .40 | +5% | 25% | NS | 11 | 9 | 9 | 6 | 5 |

Summary of data on Table A-V and Figs. A-8, 9, & 10. Differences of $\dot{Q}_{SB}$, $\dot{Q}_{F'}$, and $\dot{Q}_{PCO2}$ in reference to $\dot{Q}_F$ by direct Fick. $\bar{\Delta}$ is the mean difference in L/min. $\Delta$% is the difference between individual measurements, and SD$\Delta$% the standard deviation of differences. The significance of differences in mean $\Delta$% is given by p-value or not significant (NS).

Table A-VII. Statistical comparison of percent error between $\dot{Q}_F$ and $\dot{Q}_{SB}$ using different methods of point selection

| | Method | Mean % Error | SD of % Error |
|---|---|---|---|
| 1. | 8 or fewer points, computer restrictions on $P_{CO2}$ and R span | -12.6 | 25.1 |
| 2. | 8 points, no restrictions | -12.6 | 23.0 |
| 3. | 11 points, criteria for point selection followed | -17.2 | 15.2 |
| 4. | moving spline | -14.4 | 17.6 |

Table A-VIII

| | $\dot{V}_{O2}$ L/min | $\dot{Q}_F$ L/min | $\dot{Q}_{SB}^{sp}$ L/min | $Q_{F'}^{sp}$ L/min |
|---|---|---|---|---|
| 1. | 0.305 | 6.93 | 5.20 | 6.67 |
| 2. | 0.957 | 10.80 | 7.74 | 9.66 |
| 3. | 0.957 | 10.80 | 8.03 | 10.00 |
| 4. | 1.538 | 12.96 | 10.39 | 12.78 |
| 5. | 0.331 | 8.47 | 6.20 | 7.85 |
| 6. | 0.331 | 8.47 | 7.92 | 9.87 |
| 7. | 0.864 | 11.03 | 8.32 | 10.34 |
| 8. | 0.864 | 11.03 | 9.02 | 11.16 |
| 9. | 1.443 | 12.80 | 9.58 | 11.82 |
| 10. | 1.443 | 12.80 | 10.90 | 13.38 |
| 11. | 0.257 | 5.54 | 4.09 | 5.36 |
| 12. | 0.257 | 5.54 | 4.78 | 6.18 |
| 13. | 0.752 | 10.20 | 8.75 | 10.85 |
| 14. | 0.752 | 10.20 | 7.82 | 9.75 |
| 15. | 1.395 | 15.28 | 10.30 | 12.67 |
| 16. | 1.395 | 15.28 | 11.32 | 13.87 |
| 17. | 1.965 | 18.86 | 15.66 | 18.98 |
| 18. | 1.965 | 18.86 | 14.10 | 17.14 |
| 19. | 2.316 | 19.03 | 20.18 | 24.29 |
| 20. | 2.316 | 19.03 | 16.03 | 19.41 |
| 21. | 0.331 | 6.49 | 5.66 | 7.21 |
| 22. | 0.331 | 6.49 | 6.45 | 8.14 |
| 23. | 0.932 | 12.94 | 10.04 | 12.36 |
| 24. | 0.932 | 12.94 | 10.96 | 13.45 |
| 25. | 1.530 | 14.18 | 10.93 | 13.41 |
| 26. | 1.530 | 14.18 | 11.47 | 14.05 |
| 27. | 1.785 | 14.72 | 11.79 | 14.42 |
| 28. | 1.785 | 14.72 | 13.44 | 16.36 |
| Mean | 1.127 | 12.16 | 9.89 | 12.19 |

Oxygen consumption ($\dot{V}_{O2}$), cardiac output by the direct Fick method ($\dot{Q}_F$), the single-breath calculated with the "moving spline" technique ($\dot{Q}_{SB}^{sp}$), and the latter adjusted to predicted $\dot{Q}_{F'}^{sp}$ by the equation

$$\dot{Q}_{F'}^{sp} = 1.18\,\dot{Q}_{SB}^{sp} + .553$$

Note: With two exceptions a SB measurement was made before and after each $\dot{Q}_F$.

Table A-IX

| Method | n | $\bar{\Delta}$ L/min | $\bar{\Delta}$% | SD$\Delta$% | p | Distribution $>\dot{Q}_F$ | $<\dot{Q}_F$ | Range $<10\%$ | 10-20% | $>20\%$ |
|---|---|---|---|---|---|---|---|---|---|---|
| $\dot{Q}_{SB}^{sp}$ | 28 | -2.27 | -19% | 9% | <.001 | 1 | 27 | 4 | 11 | 13 |
| $\dot{Q}_{F'}^{sp}$ | 28 | + .03 | <1% | 11% | NS | 12 | 16 | 20 | 6 | 2 |

Summary of data on Table A-VIII and Fig. A-11. Difference in reference to $\dot{Q}_F$ of $\dot{Q}_{SB}^{sp}$ calculated by the "moving spline" technique and $\dot{Q}_{F'}^{sp}$ predicted from $\dot{Q}_{SB}^{sp}$ by the equation

$$\dot{Q}_{F'}^{sp} = 1.18\,\dot{Q}_{SB}^{sp} + .553$$

Headings are the same as in Table A-VI.

| Table A-X | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Subj. | | Work Load (kgm/min) | $Pa_{CO_2}$ | SB $Pa_{CO_2}$ | Δ 2-3 | $P\bar{v}_{CO_2}$ | SB $P\bar{v}_{CO_2}$ | Δ 5-6 | $P\bar{v}\text{-}a_{CO_2}$ | SB $P\bar{v}\text{-}a_{CO_2}$ |
| LU | 1 | 0 | 28.6 | 25.8 | 2.8 | 31.4 | 30.9 | 0.5 | 2.8 | 5.1 |
| | 2 | 300 | 31.0 | 24.4 | 6.6 | 38.6 | 36.3 | 2.3 | 7.6 | 11.9 |
| | 3 | 600 | 27.3 | 26.2 | 1.1 | 42.1 | 37.0 | 5.1 | 14.8 | 10.8 |
| | 4 | 750 | 26.4 | 25.0 | 1.4 | 43.0 | 39.9 | 3.1 | 16.6 | 14.9 |
| AT | 5 | 0 | 29.8 | 27.5 | 2.3 | 33.8 | 32.7 | 1.1 | 4.0 | 5.2 |
| | 6 | 0 | 29.8 | 26.3 | 3.5 | 33.8 | 31.1 | 2.7 | 4.0 | 4.8 |
| | 7 | 300 | 31.7 | 27.6 | 4.1 | 38.6 | 37.7 | 0.9 | 6.9 | 10.1 |
| | 8 | 300 | 31.7 | 28.5 | 3.2 | 38.6 | 37.0 | 1.6 | 6.9 | 8.5 |
| | 9 | 600 | 31.1 | 21.3 | 9.8 | 45.2 | 43.9 | 1.3 | 14.1 | 22.6 |
| | 10 | 600 | 31.1 | 17.2 | 13.9 | 45.2 | 41.2 | 4.0 | 14.1 | 24.0 |
| MY | 11 | 0 | 34.8 | 30.7 | 4.1 | 40.4 | 37.0 | 3.4 | 5.6 | 6.3 |
| | 12 | 0 | 34.8 | 30.4 | 4.4 | 40.4 | 35.3 | 5.1 | 5.6 | 4.9 |
| | 13 | 300 | 34.0 | 28.6 | 5.4 | 42.3 | 37.3 | 5.0 | 8.3 | 8.7 |
| | 14 | 300 | 34.0 | 27.7 | 6.3 | 42.3 | 38.0 | 4.3 | 8.3 | 10.3 |
| | 15 | 600 | 36.1 | 28.6 | 7.5 | 48.3 | 42.2 | 6.0 | 12.2 | 13.6 |
| | 16 | 600 | 36.1 | 28.8 | 7.3 | 48.3 | 42.8 | 5.5 | 12.2 | 14.0 |
| | 17 | 900 | 32.6 | 25.6 | 7.0 | 48.7 | 43.0 | 5.7 | 16.1 | 17.4 |
| | 18 | 900 | 32.6 | 26.4 | 6.2 | 48.7 | 43.8 | 4.9 | 16.1 | 17.4 |
| | 19 | 1050 | 30.2 | 26.4 | 3.8 | 47.1 | 41.8 | 5.3 | 16.9 | 15.4 |
| | 20 | 1050 | 30.2 | 23.7 | 6.5 | 47.1 | 42.8 | 4.3 | 16.9 | 19.1 |
| CO | 21 | 0 | 31.1 | 29.7 | 1.4 | 38.7 | 35.5 | 3.2 | 7.6 | 5.8 |
| | 22 | 0 | 31.1 | 27.6 | 3.5 | 38.7 | 33.9 | 4.8 | 7.6 | 6.3 |
| | 23 | 300 | 33.9 | 27.1 | 6.8 | 39.8 | 37.6 | 2.2 | 5.9 | 10.5 |
| | 24 | 300 | 33.9 | 27.5 | 6.4 | 39.8 | 37.1 | 2.7 | 5.9 | 9.6 |
| | 25 | 600 | 31.8 | 23.5 | 8.3 | 43.6 | 39.7 | 3.9 | 11.8 | 16.2 |
| | 26 | 600 | 31.8 | 25.8 | 6.0 | 43.6 | 39.6 | 4.0 | 11.8 | 13.8 |
| | 27 | 750 | 30.0 | 20.9 | 9.1 | 43.6 | 40.8 | 2.8 | 13.6 | 19.9 |
| | 28 | 750 | 30.0 | 24.3 | 5.7 | 43.6 | 39.9 | 3.7 | 13.6 | 15.6 |
| Mean | | | 31.7 | 26.2 | 5.5 | 42.0 | 38.4 | 3.6 | 10.3 | 12.2 |
| SD | | | 2.4 | 2.9 | p .001 | 4.5 | 3.6 | $p < .001$ | | |

| Table A-XI | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Subj. | Work kgm/min | Hb g% | Slope vol%/mm Hg | $P\bar{v}\text{-}a_{CO_2}$ mm Hg | 2 x 3 vol% | $Ca_{CO_2}$ vol% | 4 + 5 vol% | $C\bar{v}_{CO_2}$ vol% | 7 - 6 vol% | $Ca\text{-}\bar{v}_{O_2}$ vol% | 8 : 9 $R_H$ | $R_B$ | $R_E$ |
| LU 1 | 0 | 16.5 | .478 | 2.8 | 1.3 | 40.3 | 41.6 | 42.5 | 0.9 | 4.4 | 0.20 | 0.50 | 0.78 |
| 2 | 300 | 18.0 | .503 | 7.6 | 3.8 | 39.8 | 43.6 | 46.2 | 2.6 | 8.9 | 0.29 | 0.72 | 0.79 |
| 3 | 600 | 18.4 | .509 | 14.8 | 7.5 | 34.0 | 41.5 | 45.2 | 3.7 | 11.9 | 0.31 | 0.94 | 0.91 |
| 4 | 750 | 19.0 | .519 | 16.6 | 8.6 | 30.4 | 39.0 | 43.5 | 4.5 | 13.2 | 0.34 | 0.99 | 0.93 |
| AT 5 | 0 | 16.1 | .472 | 4.0 | 1.9 | 40.6 | 42.5 | 43.1 | 0.6 | 3.9 | 0.15 | 0.64 | 0.85 |
| 6 | 300 | 17.5 | .495 | 6.9 | 3.4 | 40.9 | 44.3 | 46.8 | 2.5 | 7.9 | 0.32 | 0.75 | 0.79 |
| 7 | 600 | 18.2 | .506 | 14.1 | 7.1 | 36.1 | 43.2 | 46.5 | 3.3 | 11.3 | 0.29 | 0.92 | 1.03 |
| MY 8 | 0 | 15.7 | .465 | 5.6 | 2.6 | 46.3 | 48.9 | 48.9 | 0 | 4.6 | -- | 0.57 | 0.89 |
| 9 | 300 | 16.2 | .474 | 8.3 | 3.9 | 45.3 | 49.2 | 50.3 | 1.1 | 7.4 | 0.15 | 0.68 | 0.80 |
| 10 | 600 | 16.5 | .478 | 12.2 | 5.8 | 45.5 | 51.3 | 52.7 | 1.4 | 9.1 | 0.15 | 0.79 | 0.83 |
| 11 | 900 | 16.9 | .485 | 16.1 | 7.8 | 40.4 | 48.2 | 50.3 | 2.1 | 10.5 | 0.20 | 0.94 | 0.92 |
| 12 | 1050 | 16.9 | .485 | 16.9 | 8.2 | 37.5 | 45.7 | 49.1 | 3.4 | 12.2 | 0.28 | 0.95 | 0.94 |
| CO 13 | 0 | 16.8 | .483 | 7.6 | 3.7 | 42.2 | 45.9 | 46.2 | 0.3 | 5.1 | 0.06 | 0.78 | 0.87 |
| 14 | 300 | 17.9 | .501 | 5.9 | 3.0 | 42.7 | 45.7 | 48.3 | 2.6 | 7.2 | 0.36 | 0.78 | 0.83 |
| 15 | 600 | 18.3 | .508 | 11.8 | 6.0 | 39.0 | 45.0 | 48.3 | 3.3 | 10.8 | 0.31 | 0.86 | 0.88 |
| 16 | 750 | 17.8 | .500 | 13.6 | 6.8 | 37.7 | 44.5 | 48.5 | 4.0 | 12.2 | 0.33 | 0.89 | 0.90 |
| DE 17 | 0 | 16.1 | .472 | 2.5 | 1.2 | 43.0 | 44.2 | 45.1 | 0.9 | 3.2 | 0.28 | 0.66 | 0.92 |
| 18 | 300 | 16.4 | .477 | 10.4 | 5.0 | 42.4 | 47.4 | 48.8 | 1.4 | 8.3 | 0.17 | 0.77 | 0.73 |
| 19 | 600 | 17.1 | .488 | 15.9 | 7.8 | 35.6 | 43.4 | 46.8 | 3.4 | 11.8 | 0.29 | 0.95 | 0.98 |
| 20 | 900 | 18.0 | .503 | 21.7 | 10.9 | 26.4 | 37.3 | 41.8 | 4.5 | 14.5 | 0.31 | 1.06 | 1.06 |
| Mean | | 17.2 | .490 | 10.8 | 5.3 | 39.3 | 44.6 | 46.9 | 2.3 | 8.9 | 0.26 | 0.85 | 0.88 |
| SD | | | .015 | | | | | | | | 0.08 | 0.15 | 0.08 |

The slope of the $CO_2$ combining curve (col. 2) is calculated from Hb concentration (col. 1) by the equation $S = .0163Hb + .21$. The slope is multiplied by the difference $P\bar{v}_{CO_2} - Pa_{CO_2}$ (col. 3) and the product (col. 4) added to the arterial $CO_2$ content (col. 5) to obtain the $CO_2$ content at the point where the arterial curve intersects $P\bar{v}_{CO_2}$ (col. 6). The difference in $CO_2$ content between this point and mixed venous blood (col. 7) reflects the Haldane effect (col. 8), and when divided by the arterio-venous $O_2$ difference (col. 9) gives $R_H$ (col. 10).

## B. OPTIMUM PROTOCOL FOR THE ASSESSMENT OF CARDIO-RESPIRATORY COMPETENCE

A large variety of exercise tests have been used to evaluate the response of the respiratory and circulatory systems to exercise. The determination of maximum aerobic power is considered to be the most reliable index of an individual's physical fitness. Direct measurement is based on performing exercise with increasing intensity and establishing a work rate above which a further increase in work output does not bring about a higher oxygen uptake. This procedure is time consuming because it requires repetitive testing over several days and reliable results are not always obtainable in subjects not used to exerting themselves excessively. Indirect measurement is based on establishing a linear relationship between heart rate and oxygen uptake at two or more submaximum levels of work and extrapolating to an assumed maximal heart rate. The latter procedure is most commonly used clinically on patients to whom maximal exertion might be harmful. Obviously, the indirect method provides more valid results once the individual's maximal heart rate has been established previously by the direct method. Therefore it is particularly useful for serial studies to monitor an individual's cardio-respiratory competence during and after unusual environmental stress, such as prolonged space flight, where lack of terrestrial gravitation and/or of physical activity may have a deconditioning effect on the cardiovascular system.

The following study was undertaken to establish an exercise protocol best suited for use as a standard physical fitness test to be performed periodically in the course of space operations of longer duration as well as before and after flight. The choice of the procedure described below was based on experience gained in this laboratory over the past 16 years in many hundreds of physical competence tests, including the astronaut candidates from whom the original seven Mercury astronauts were chosen in 1959 ( 6 ). A similar protocol was used in a study on physiological aging in over 500 commercial pilots, 25-65 years of age, at the Lovelace Foundation ( 7 ), and in a continuing investigation on a smaller number of NASA test pilots who have been tested annually in this laboratory for a period of more than ten years ( 8 ).

Procedure:

The exercise is performed on a bicycle ergometer [Von Döbeln (2 )] on which the brake load can be adjusted in steps of 75 kgm/min over a range from 75 to 2100 kgm/min. The standard pedalling rate is 50 rpm given by metronome. The exercise profile follows a ramp pattern as shown at the bottom of Fig. B-1. The initial work load for men is 300 kgm/min and this is maintained for four minutes for warm-up and to measure metabolic rate and cardiac output. Throughout the entire test and for five minutes of recovery the ECG is visualized on an oscilloscope and heart rate indicated on a cardiotachometer. During the latter part of each minute, ECG and blood pressure are recorded with a Sanborn (Model 67-1600) electrocardiograph and an automatic blood pressure monitoring system (AIRESEARCH). In the third minute expired air is collected via a Lloyd respiratory valve into a meteorological balloon for volume measurements and analysis by mass-spectrometer (MEDSPECT, MMS-8) calibrated with gas mixtures analyzed by the Scholander method. Immediately after completing the third minute, the subject performs a slow, deep expiration after inspiring somewhat deeper than usual to provide a single-breath (SB) record by mass-spectrometer on an X-Y recorder (Bryans Autoplotter 22000) for estimation of cardiac output in conjunction with the preceding metabolic rate measurement. During the remainder of the fourth minute the subject overcomes the hyperpnea following the protracted breath and reverts to his normal breathing pattern. Beginning with the fifth minute the brake load is increased each minute by 75 kgm/min until 600 kgm/min is reached at the seventh minute, whereupon another bag is collected followed by another SB maneuver at the beginning of the eighth minute. The work load is increased at the beginning of the ninth minute, again by 75 kgm/min, and each subsequent minute up to 900 kgm/min at 13 minutes where another bag collection is made immediately followed by an SB. Exactly the same sequence is followed from the 15-18th minute adding another 300 kgm/min. Depending upon the work capacity of the subject, additional measurements can be made at intervals of 75 kgm/min (one minute) or 150 kgm/min (2 minutes). A minimum of three measurements (300, 600, and 900 kgm/min) are required to establish the heart rate-oxygen consumption relationship for an indirect estimate of maximum aerobic power. On the other hand, the same protocol can be continued with minute-by-minute increments of 75 kgm/min until the subject

is no longer able to maintain the pedalling rhythm to assess maximal work capacity directly. It is advisable to collect bags every minute after a heart rate of 160 has been reached to ensure that a measurement is obtained in the last minute. SB maneuvers with the subsequent additional minute are optional beyond the 18th minute and become increasingly difficult to perform with rising ventilatory requirements. Previously the six subjects engaged in this study had each established their aerobic capacity and maximal heart rate. Then each completed three tests using the indirect approach in which cardiac output was determined at 4-5 levels of submaximal exercise. In a series of preliminary tests several cardiac output determinations were performed at the same work load to find out if there was much change after the initial measurements in the first and second minute at a given work level. Repetitive cardiac output determinations were made after four minutes at rest, 25% and 50% of $\dot{V}_{O2\ max}$ on four subjects and also after six minutes at 75% $\dot{V}_{O2\ max}$ (Table B-II).

In all estimates of cardiac output ($\dot{Q}$) in this study the moving spline technique was applied to the single-breath record and the predicted direct Fick value obtained by the regression equation (11) in Part A.

Results and comments:

In view of the fact that in the proposed test protocol the work load is increased by a small amount every minute, there was some question whether a cardiac output determination at the end of the first minute after reaching a given level of work would be representative of cardiac activity at that point or whether it would be necessary to wait for a longer period of time until a "steady-state" was reached. Earlier work by Donald, et. al. ( 3 ) indicates that oxygen uptake and cardiac output achieves a steady-state after as little as 1-1/2 minutes on starting heavy work from rest. Considering the relatively small increments of work employed in our tests, it was anticipated that valid measurements of $\dot{Q}$ could be obtained in the second minute. The results of the repetitive determinations after four and six minutes at different work loads up to 75% of maximum aerobic power shown in Table B-II for four subjects confirmed this contention. Although there was a tendency for $\dot{Q}$ to increase in the fourth and sixth minute after reaching the new work level, the mean difference was less than +3% and was not statistically

significant. Consequently, the single-breath maneuver was performed in the second minute after increasing the brake load as indicated in Fig. B-1 in the final protocol. In this manner the duration of the test could be kept within reasonable limits.

Table B-III contains complete data for the three separate tests performed by each subject arranged according to work intensity. All subjects performed at 300, 600, and 900 kgm/min. The subsequent higher work loads at which measurements were made were chosen according to the individual subject's work capacity so as to achieve 75-80% of maximal aerobic power at the highest work level. Thus subjects LO and MY continued up to 1350 kgm/min where their $\dot{V}_{O2}$ was 78% and 81% maximal, respectively, whereas subjects CO, JA, and LU were at 76-77% of maximal $\dot{V}_{O2}$ working at 1050 kgm/min.

A glance at the results of the three separate tests at each work level in Table B-III shows remarkably close agreement for ventilatory, metabolic, and circulatory responses considering that the tests were performed several days apart.

A summary of mean values and standard deviations are tabulated in Table B-IV for all items measured or derived for six different work intensities including rest. The coefficients of variation in the last column show much greater variation at rest than at the higher work intensities. This is not surprizing because no attempt was made to induce basal metabolic conditions, and measurements were made sitting on the bicycle ergometer with mixed emotions on the part of the subjects in anticipation of the test. As the exercise progressed, however, the variance became much smaller even considering the differences in size, age, and physical fitness among the subjects.

Fig. B-1 summarizes the mean values for respiratory, metabolic, and cardiovascular functions at rest and in the course of five progressive levels of work. The standard test protocol is apparent from the work diagram at the foot of the chart with the points of measurement indicated as $\dot{Q}$. In general, oxygen consumption ($\dot{V}_{O2}$), heart rate (HR), cardiac output ($\dot{Q}$), and the arterio-venous oxygen difference ($AVD_{O2}$) closely parallel the increments in work, whereas ventilation ($\dot{V}_I$) and respiratory exchange ratio (R) increase more markedly above 50% of maximal aerobic power. It is noteworthy that the stroke volume ($V_s$) shows a rise of 46% between rest and the first exercise

step, but increases by only 6% in the further course of the exercise. This is in contrast to our observations during exercise in the supine position shown in Fig. A-3, where there was no consistent change in stroke volume at the onset of exercise. In either the supine or the sitting posture the continued increase in cardiac output with higher work loads is apparently almost entirely attributable to the rising heart rate.

A comparison of the results of determinations of cardiac output by the single-breath method as a function of metabolic rate in this study with those of other investigators using invasive methods is presented in Fig. B-2 in the form of regression lines: $\dot{Q}$ versus $\dot{V}_{O2}$. Line #1 was obtained by Ekelund and Holmgren ( 4 ) from 140 measurements for rest and exercise in the supine position with the direct Fick procedure. Similarly, line #2 describes the results of Gattiker ( 5 ) from 52 determinations on normal subjects working supine (Fick method). Åstrand, et. al. ( 1 ) reported regression #4 from 126 points for work sitting on a bicycle ergometer at work loads up to 70% of maximum. Their data were obtained by the dye-dilution method. Line #3 represents the present study with 95 points ranging up to 80% $\dot{V}_{O2\,max}$ also sitting on a bicycle. The slopes of all four regression lines are practically identical, amounting to approximately 6 L/min increase in cardiac output for every one L/min rise in $\dot{V}_{O2}$. The zero intercept is generally higher in supine exercise.

Finally, the validity of the indirect determination of maximal aerobic power as estimated by extrapolation from the heart rate-metabolic rate relationship in submaximal exercise following the protocol of this study was tested. For this purpose regression equations for oxygen consumption versus heart rate were calculated from the three submaximal tests on each subject and solved for predicted maximal aerobic power at the maximum heart rate previously determined directly. The results are shown below.

| | $\dot{V}_{O2\,max}$ (L/min) | | | |
|---|---|---|---|---|
| Subj. | direct | indirect | difference | Δ% |
| LO | 3.645 | 3.650 | +.005 | <1% |
| MY | 3.612 | 2.930 | -.682 | -19% |
| BR | 3.274 | 3.406 | +.132 | + 4% |
| CO | 2.879 | 2.402 | -.477 | -17% |
| JA | 2.737 | 2.213 | -.524 | -19% |
| LU | 2.971 | 2.869 | -.102 | - 3% |
| Mean | 3.186 | 2.912 | -.275 | - 9% |

Only in one subject was there an ideal agreement between direct and indirect estimation of aerobic power. In the other subjects the indirect measure was less than the direct in four out of five instances. The mean difference was - 9% and this was not statistically significant, but the difference was quite large in three subjects. It would appear that the indirect estimation of aerobic power is not a very good substitute for the direct measurement, even when the maximal heart rate of the subject is known. Nevertheless, the proposed submaximal exercise protocol, on its own merits, provides a valuable means of evaluating cardio-respiratory competence under dynamic conditions and would lend itself well to the periodic testing of astronauts.

Summary:

An exercise protocol for the periodic assessment of cardio-pulmonary competence in astronauts is proposed which consists of exercise of progressive intensity following a ramp pattern with increments of 75 kgm/min starting from a baseline of 300 kgm/min. Heart rate and blood pressure are monitored minute-by-minute while metabolic rate and cardiac output are determined at 300, 600, and 900 kgm/min which is in the 3rd, 8th, and 13th minutes of the test. Depending upon the capability of the subject, additional measurements can be added after two or more increments in work load. The protocol can be used equally well for the determination of aerobic capacity by continuing the test with increments of 75 kgm/min until the subject is no longer able to maintain the pedalling rhythm. A complete profile is thus obtained of the dynamic response of the cardiovascular and respiratory systems from rest through mild and submaximal to maximal exercise if desired. Results of this type of test are presented on six subjects who performed the test on three different occasions to demonstrate the range of variation within and between individuals of different ages and physical conditions. The values obtained for cardiac output and its component functions, stroke volume, and arterio-venous oxygen difference compare favorably with those reported in the literature from direct determinations by the Fick and dye-dilution methods during exercise. Preliminary tests had shown that cardiac output determinations performed at four and six minutes at a given work load are not statistically different from the initial measurement after the first minute.

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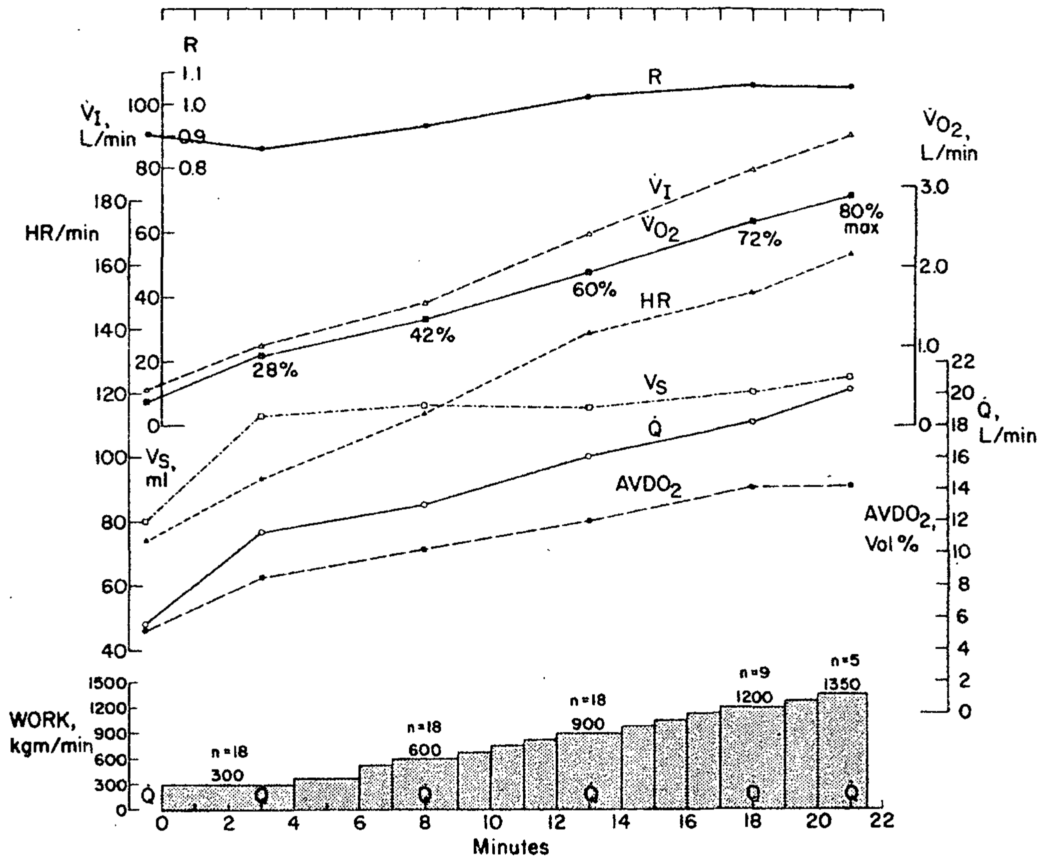


Fig. B-1. Respiratory and cardiovascular functions in the course of graded submaximal exercise following a ramp pattern with steps of 75 kgm/min and periodic measurements of respiratory gas exchange and cardiac output ($\dot{Q}$). Mean values are plotted for 3 different tests on 6 subjects at rest, 300, 600, and 900 kgm/min with fewer points (n) at 1200 and 1350 kgm/min. Percent of maximal aerobic power (means) is given on $\dot{V}_{O2}$ curve.

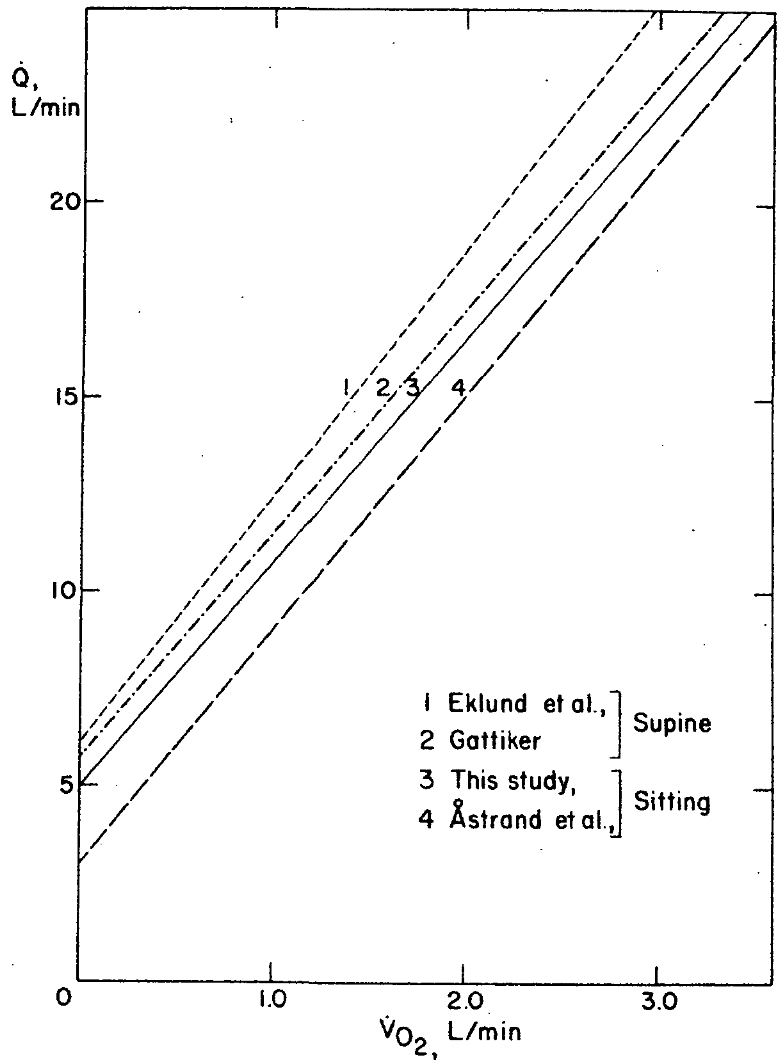


Fig. B-2. Regression lines for cardiac output versus metabolic rate ($\dot{V}_{O2}$)

| | Source (ref.) | n | Posture | Method | Regression | SE |
|---|---|---|---|---|---|---|
| 1. | Ekelund (4) | 140 | supine | Fick | $\dot{Q} = 6.30\,\dot{V}_{O2} + 6.17$ | 1.36 |
| 2. | Gattiker (5) | 52 | supine | Fick | $\dot{Q} = 5.78\,\dot{V}_{O2} + 5.70$ | 1.90 |
| 3. | Present Study | 95 | sitting | SB | $\dot{Q} = 5.77\,\dot{V}_{O2} + 4.98$ | 1.89 |
| 4. | Åstrand (1) | 126 | sitting | Dye-Dil. | $\dot{Q} = 6.01\,\dot{V}_{O2} + 3.07$ | -- |

Table B-I. Physical characteristics of subjects

| Subj. | Age years | Height cm | Weight kg | $\dot{V}_{O2}$ max L/min | $\dot{V}_{O2}$ max ml/min/kg | Max. HR per min |
|---|---|---|---|---|---|---|
| LO | 28 | 178 | 70.0 | 3.645 | 52.1 | 186 |
| MY | 36 | 188 | 78.8 | 3.612 | 45.8 | 177 |
| BR | 37 | 168 | 60.1 | 3.274 | 54.5 | 178 |
| CO | 18 | 166 | 56.0 | 2.879 | 51.4 | 198 |
| JA | 30 | 172 | 62.6 | 2.737 | 43.7 | 173 |
| LU | 62 | 180 | 81.0 | 2.971 | 36.7 | 168 |

Table B-II. Repetitive Cardiac Output Determinations

| | Rest ① | Rest ② | Rest ② - ① Δ% | 25% $\dot{V}_{O2}$ max ① | 25% $\dot{V}_{O2}$ max ② | 25% $\dot{V}_{O2}$ max ② - ① Δ% | 50% $\dot{V}_{O2}$ max ① | 50% $\dot{V}_{O2}$ max ② | 50% $\dot{V}_{O2}$ max ② - ① Δ% |
|---|---|---|---|---|---|---|---|---|---|
| LU | 6.43 | 8.18 | +27% | 12.73 | 10.44 | -18% | 13.17 | 12.54 | -5% |
| MY | 4.19 | 4.97 | +19% | 12.36 | 11.31 | - 8% | 15.04 | 16.54 | +10% |
| LO | 4.19 | 4.90 | +17% | 9.37 | 7.61 | -19% | 13.80 | 18.14 | +31% |
| CO | 4.23 | 4.28 | + 1% | 8.88 | 8.67 | - 2% | 12.25 | 14.05 | +15% |

75% $\dot{V}_{O2}$ max

| | ① | ② | ③ | ② - ① Δ% | ③ - ① Δ% |
|---|---|---|---|---|---|
| LU | 15.20 | 15.79 | 16.60 | +4% | +9% |
| MY | 19.42 | 18.17 | 18.43 | -6% | -5% |
| LO | 27.38 | 27.46 | 31.40 | 0% | +15% |
| CO | 14.56 | 14.83 | 15.19 | +2% | + 4% |

① is the first measurement at rest or after one minute at each of three levels of exercise. ② is after four minutes and ③ after six minutes at the same level of activity. The mean difference between the first and second, and first and third measurement was less than 3% and not statistically significant.

Table B-III. Individual data at rest and during exercise for three different tests on each subject

Subject : LO

| Work (kgm/min) | No. | $\dot{V}_{O2}$ L/min | R | $\dot{V}_I$ L/min | $\dot{Q}$ L/min | HR per min | $V_s$ ml | $AVD_{O2}$ vol% |
|---|---|---|---|---|---|---|---|---|
| Rest | 1 | .263 | .80 | 8.20 | 4.66 | 72 | 65 | 5.6 |
| " | 2 | .296 | .78 | 8.78 | 5.45 | 71 | 77 | 5.4 |
| " | 3 | .305 | .81 | 8.93 | 4.93 | 89 | 55 | 6.2 |
| 8% | Mean | .288 | .80 | 8.64 | 5.01 | 77 | 66 | 5.7 |
| 300 | 1 | .826 | .82 | 22.38 | 9.02 | 90 | 100 | 9.2 |
| " | 2 | .927 | .80 | 23.16 | 8.88 | 92 | 97 | 10.4 |
| " | 3 | .782 | .83 | 20.12 | 7.56 | 96 | 79 | 10.3 |
| 23% | Mean | .845 | .82 | 21.89 | 8.49 | 93 | 92 | 10.0 |
| 600 | 1 | 1.265 | .86 | 32.75 | 10.72 | 100 | 107 | 11.8 |
| " | 2 | 1.240 | .88 | 32.10 | 10.80 | 106 | 102 | 11.5 |
| " | 3 | 1.229 | .90 | 31.30 | 10.80 | 111 | 97 | 11.4 |
| 34% | Mean | 1.245 | .88 | 32.05 | 10.77 | 106 | 102 | 11.6 |
| 900 | 1 | 1.836 | 1.02 | 57.29 | 14.69 | 121 | 121 | 12.5 |
| " | 2 | 1.871 | .95 | 49.48 | 12.76 | 126 | 101 | 14.7 |
| " | 3 | 1.881 | .97 | 48.45 | 16.92 | 133 | 127 | 11.1 |
| 51% | Mean | 1.863 | .98 | 51.74 | 14.79 | 127 | 116 | 12.8 |
| 1200 | 1 | 2.478 | 1.04 | 77.23 | 17.02 | 149 | 114 | 14.6 |
| " | 2 | 2.423 | 1.04 | 76.13 | 20.20 | 148 | 136 | 12.0 |
| " | 3 | 2.473 | 1.04 | 69.61 | 17.86 | 145 | 123 | 13.8 |
| 67% | Mean | 2.458 | 1.04 | 74.32 | 18.36 | 147 | 124 | 13.5 |
| 1350 | 1 | 2.883 | 1.04 | 89.32 | 18.17 | 160 | 114 | 15.9 |
| " | 2 | 2.841 | 1.06 | 87.57 | 18.56 | 159 | 117 | 15.3 |
| " | 3 | 2.836 | 1.07 | 88.21 | 22.10 | 156 | 142 | 12.9 |
| 78% | Mean | 2.853 | 1.06 | 88.37 | 19.61 | 158 | 124 | 14.7 |

Table B-III. (Cont.)

Subject : JA

| Work (kgm/min) | No. | $\dot{V}_{O2}$ L/min | R | $\dot{V}_I$ L/min | $\dot{Q}$ L/min | HR per min | $V_s$ ml | $AVD_{O2}$ vol% |
|---|---|---|---|---|---|---|---|---|
| Rest | 1 | .359 | 1.36 | 21.51 | 7.48 | 86 | 87 | 4.8 |
| " | 2 | .372 | 1.28 | 19.93 | 8.24 | 82 | 100 | 4.5 |
| " | 3 | .395 | 1.46 | 30.20 | 9.58 | 84 | 114 | 4.1 |
| 14% | Mean | .375 | 1.37 | 23.88 | 8.43 | 84 | 100 | 4.5 |
| 300 | 1 | .904 | .88 | 28.88 | 12.26 | 90 | 136 | 7.4 |
| " | 2 | .927 | .90 | 30.12 | 9.59 | 95 | 101 | 9.7 |
| " | 3 | .833 | .91 | 26.63 | 7.98 | 96 | 83 | 10.4 |
| 32% | Mean | .888 | .90 | 28.54 | 9.94 | 94 | 107 | 9.2 |
| 600 | 1 | 1.193 | 1.10 | 43.13 | 11.93 | 120 | 99 | 10.0 |
| " | 2 | 1.341 | 1.03 | 45.93 | 14.76 | 126 | 117 | 9.1 |
| " | 3 | 1.324 | 1.03 | 44.94 | 13.67 | 123 | 111 | 9.7 |
| 47% | Mean | 1.286 | 1.05 | 44.67 | 13.45 | 123 | 109 | 9.6 |
| 900 | 1 | 1.730 | 1.06 | 60.43 | 17.49 | 150 | 117 | 9.9 |
| " | 2 | 1.751 | 1.02 | 58.61 | 14.78 | 145 | 102 | 11.8 |
| " | 3 | 1.929 | 1.03 | 64.79 | 18.33 | 154 | 119 | 10.5 |
| 66% | Mean | 1.803 | 1.04 | 62.28 | 16.87 | 150 | 113 | 10.7 |
| 1050 | 1 | 2.089 | 1.07 | 78.18 | 18.25 | 163 | 112 | 11.4 |
| " | 2 | 2.148 | 1.04 | 73.89 | 19.75 | 158 | 125 | 10.9 |
| " | 3 | 2.049 | 1.07 | 72.63 | 17.60 | 165 | 107 | 11.6 |
| 77% | Mean | 2.095 | 1.06 | 74.90 | 18.53 | 162 | 115 | 11.3 |

Table B-III. (Cont.)

Subject : MY

| Work (kgm/min) | No. | $\dot{V}_{O2}$ L/min | R | $\dot{V}_I$ L/min | $\dot{Q}$ L/min | HR per min | $V_s$ ml | $AVD_{O2}$ vol% |
|---|---|---|---|---|---|---|---|---|
| Rest | 1 | .279 | .87 | 7.02 | 4.02 | 58 | 69 | 6.9 |
| " | 2 | .305 | .90 | 7.60 | 7.19 | 56 | 128 | 4.2 |
| " | 3 | .223 | .98 | 6.99 | 4.93 | 61 | 81 | 4.5 |
| 7% | Mean | .269 | .92 | 7.20 | 5.38 | 58 | 93 | 5.2 |
| 300 | 1 | .872 | .83 | 20.37 | 13.41 | 83 | 162 | 6.5 |
| " | 2 | .945 | .85 | 21.66 | 14.07 | 83 | 170 | 6.7 |
| " | 3 | .888 | .80 | 19.33 | 13.13 | 85 | 154 | 6.8 |
| 25% | Mean | .902 | .83 | 20.45 | 13.54 | 84 | 162 | 6.7 |
| 600 | 1 | 1.410 | .92 | 35.91 | 18.36 | 107 | 172 | 7.7 |
| " | 2 | 1.347 | .88 | 30.96 | 14.66 | 112 | 131 | 9.2 |
| " | 3 | 1.374 | .85 | 30.44 | 14.75 | 104 | 142 | 9.3 |
| 38% | Mean | 1.377 | .88 | 32.44 | 15.92 | 108 | 148 | 8.7 |
| 900 | 1 | 2.069 | .99 | 57.97 | 16.59 | 140 | 119 | 12.5 |
| " | 2 | 1.981 | .95 | 48.32 | 16.24 | 133 | 122 | 12.2 |
| " | 3 | 1.827 | .94 | 43.88 | 16.63 | 132 | 126 | 11.0 |
| 54% | Mean | 1.959 | .96 | 50.06 | 16.49 | 135 | 122 | 11.9 |
| 1200 | 1 | 2.556 | 1.04 | 82.70 | 19.30 | 167 | 116 | 13.2 |
| " | 2 | 2.556 | 1.05 | 79.45 | 18.66 | 162 | 115 | 13.7 |
| " | 3 | 2.557 | 1.03 | 76.91 | 16.24 | 156 | 104 | 15.7 |
| 71% | Mean | 2.556 | 1.04 | 79.69 | 18.07 | 162 | 112 | 14.2 |
| 1350 | 1 | 2.925 | 1.06 | 96.95 | 21.12 | 171 | 124 | 13.8 |
| " | 2 | 2.904 | 1.05 | 89.70 | 21.64 | 169 | 128 | 13.4 |
| 81% | Mean | 2.915 | 1.06 | 93.33 | 21.38 | 170 | 126 | 13.6 |

Table B-III. (Cont.)

Subject : BR

| Work (kgm/min) | No. | $\dot{V}_{O2}$ L/min | R | $\dot{V}_I$ L/min | $\dot{Q}$ L/min | HR per min | $V_s$ ml | $AVD_{O2}$ vol% |
|---|---|---|---|---|---|---|---|---|
| Rest | 1 | .244 | .82 | 7.26 | 4.57 | 50 | 91 | 5.3 |
| " | 2 | .222 | .87 | 6.99 | 5.32 | 61 | 87 | 4.2 |
| " | 3 | .213 | .86 | 6.33 | 3.35 | 51 | 66 | 6.4 |
| 7% | Mean | .226 | .85 | 6.86 | 4.41 | 54 | 81 | 5.3 |
| 300 | 1 | .909 | .86 | 23.90 | 9.01 | 79 | 114 | 10.1 |
| " | 2 | .804 | .89 | 21.33 | 8.27 | 75 | 110 | 9.7 |
| " | 3 | .765 | .87 | 21.02 | 8.53 | 68 | 125 | 9.0 |
| 25% | Mean | .826 | .87 | 22.08 | 8.60 | 74 | 116 | 9.6 |
| 600 | 1 | 1.308 | .90 | 33.05 | 10.72 | 96 | 112 | 12.2 |
| " | 2 | 1.270 | .97 | 34.68 | 12.14 | 96 | 126 | 10.5 |
| " | 3 | 1.267 | .94 | 32.34 | 10.93 | 94 | 116 | 11.6 |
| 39% | Mean | 1.282 | .94 | 33.36 | 11.26 | 95 | 118 | 11.4 |
| 900 | 1 | 1.917 | .98 | 51.82 | 15.15 | 118 | 128 | 12.7 |
| " | 2 | 1.970 | 1.03 | 55.83 | 16.00 | 121 | 132 | 12.3 |
| " | 3 | 1.812 | 1.04 | 53.50 | 16.42 | 114 | 144 | 11.0 |
| 58% | Mean | 1.900 | 1.02 | 53.72 | 15.86 | 118 | 135 | 12.0 |
| 1200 | 1 | 2.722 | 1.02 | 80.06 | 22.59 | 142 | 159 | 12.0 |
| " | 2 | 2.518 | 1.13 | 91.13 | 15.77 | 148 | 107 | 16.0 |
| " | 3 | 2.495 | 1.11 | 85.07 | 16.54 | 140 | 118 | 15.1 |
| 79% | Mean | 2.578 | 1.09 | 85.42 | 18.30 | 143 | 128 | 14.4 |

Table B-III. (Cont.)

Subject : CO

| Work (kgm/min) | No. | $\dot{V}_{O2}$ L/min | R | $\dot{V}_I$ L/min | $\dot{Q}$ L/min | HR per min | $V_s$ ml | $AVD_{O2}$ vol% |
|---|---|---|---|---|---|---|---|---|
| Rest | 1 | .260 | .78 | 7.13 | 5.73 | 75 | 76 | 4.5 |
| " | 2 | .279 | .73 | 7.37 | 6.04 | 69 | 88 | 4.6 |
| " | 3 | .265 | .78 | 7.59 | 5.39 | 77 | 70 | 4.9 |
| 9% | Mean | .268 | .76 | 7.36 | 5.72 | 74 | 78 | 4.7 |
| 300 | 1 | .870 | .83 | 24.14 | 14.56 | 104 | 140 | 6.0 |
| " | 2 | .868 | .81 | 23.61 | 12.03 | 92 | 131 | 7.2 |
| " | 3 | .801 | .84 | 22.44 | 12.36 | 111 | 111 | 6.5 |
| 29% | Mean | .846 | .83 | 23.40 | 12.98 | 102 | 127 | 6.6 |
| 600 | 1 | 1.214 | .91 | 34.72 | 12.04 | 121 | 100 | 10.1 |
| " | 2 | 1.348 | .93 | 38.44 | 14.58 | 135 | 108 | 9.2 |
| " | 3 | 1.285 | .91 | 36.55 | 15.87 | 132 | 120 | 8.1 |
| 45% | Mean | 1.282 | .92 | 34.57 | 14.16 | 129 | 109 | 9.1 |
| 900 | 1 | 1.881 | 1.07 | 61.43 | 14.39 | 171 | 84 | 13.1 |
| " | 2 | 1.933 | 1.04 | 60.18 | 17.27 | 163 | 106 | 11.2 |
| " | 3 | 1.765 | 1.00 | 51.95 | 15.81 | 162 | 98 | 11.2 |
| 65% | Mean | 1.859 | 1.04 | 57.85 | 15.82 | 165 | 96 | 11.8 |
| 1050 | 1 | 2.046 | 1.10 | 72.77 | 18.85 | 182 | 104 | 10.9 |
| " | 2 | 2.251 | 1.10 | 82.38 | 19.18 | 182 | 105 | 11.7 |
| " | 3 | 2.251 | 1.08 | 75.99 | 19.70 | 177 | 111 | 11.4 |
| 76% | Mean | 2.182 | 1.09 | 77.04 | 19.24 | 180 | 107 | 11.3 |

Table B-III. (Cont.)

Subject : LU

| Work (kgm/min) | No. | $\dot{V}_{O2}$ L/min | R | $\dot{V}_I$ L/min | $\dot{Q}$ L/min | HR per min | $V_s$ ml | $AVD_{O2}$ vol% |
|---|---|---|---|---|---|---|---|---|
| Rest | 1 | .404 | .75 | 12.74 | 6.63 | 95 | 70 | 6.1 |
| " | 2 | .343 | .76 | 10.15 | 5.62 | 90 | 62 | 6.1 |
| " | 3 | .365 | .79 | 12.60 | 5.12 | 96 | 53 | 7.1 |
| 12% | Mean | .371 | .77 | 11.83 | 5.79 | 94 | 62 | 6.4 |
| 300 | 1 | 1.017 | .91 | 36.71 | 11.51 | 114 | 101 | 8.8 |
| " | 2 | .900 | .84 | 29.98 | 10.00 | 106 | 94 | 9.0 |
| " | 3 | .892 | .93 | 33.64 | 10.39 | 111 | 94 | 8.6 |
| 32% | Mean | .936 | .89 | 33.44 | 10.63 | 110 | 96 | 8.8 |
| 600 | 1 | 1.393 | .95 | 50.95 | 12.76 | 122 | 105 | 10.9 |
| " | 2 | 1.344 | .87 | 44.56 | 11.89 | 118 | 101 | 11.3 |
| " | 3 | 1.459 | .93 | 50.72 | 14.34 | 121 | 119 | 10.2 |
| 47% | Mean | 1.399 | .92 | 48.74 | 13.00 | 120 | 108 | 10.8 |
| 900 | 1 | 2.005 | 1.07 | 86.08 | 17.94 | 140 | 128 | 11.2 |
| " | 2 | 1.969 | 1.03 | 80.28 | 15.04 | 133 | 113 | 13.1 |
| " | 3 | 1.995 | 1.08 | 85.79 | 14.77 | 141 | 105 | 13.5 |
| 67% | Mean | 1.990 | 1.06 | 84.05 | 15.92 | 138 | 115 | 12.6 |
| 1050 | 1 | 2.281 | 1.17 | 119.17 | 18.45 | 151 | 122 | 12.4 |
| " | 2 | 2.265 | 1.19 | 142.21 | 16.96 | 149 | 114 | 13.4 |
| " | 3 | 2.245 | 1.13 | 116.95 | 21.42 | 152 | 141 | 10.5 |
| 76% | Mean | 2.264 | 1.16 | 126.11 | 18.94 | 151 | 126 | 12.1 |

Table B-IV. Summary of results of all exercise tests with means and standard deviations for each item measured

| Work (kgm/min) | Subj. | Tests | % $\dot{V}_{O2}$ max | Mean | SD | coeff. var. |
|---|---|---|---|---|---|---|
| Oxygen Consumption (L/min) | | | | | | |
| Rest | 6 | 18 | 9% | .299 | .062 | 21% |
| 300 | 6 | 18 | 28% | .874 | .064 | 7% |
| 600 | 6 | 18 | 42% | 1.312 | .072 | 5% |
| 900 | 6 | 18 | 60% | 1.896 | .095 | 5% |
| 1050 | 3 | 9 | 76% | 2.181 | .098 | 4% |
| 1200 | 3 | 9 | 72% | 2.531 | .085 | 3% |
| 1350 | 2 | 5 | 80% | 2.878 | .039 | 1% |
| Ventilation (L/min) | | | | | | |
| Rest | 6 | 18 | 9% | 10.96 | 6.50 | 59% |
| 300 | 6 | 18 | 28% | 24.97 | 4.96 | 20% |
| 600 | 6 | 18 | 42% | 37.97 | 6.90 | 18% |
| 900 | 6 | 18 | 60% | 59.78 | 12.43 | 20% |
| 1050 | 3 | 9 | 76% | 92.69 | 26.20 | 28% |
| 1200 | 3 | 9 | 72% | 79.81 | 6.09 | 8% |
| 1350 | 2 | 5 | 80% | 90.35 | 3.79 | 4% |
| Respiratory Exchange Ratio | | | | | | |
| Rest | 6 | 18 | 9% | 0.91 | 0.22 | 24% |
| 300 | 6 | 18 | 28% | 0.86 | 0.04 | 5% |
| 600 | 6 | 18 | 42% | 0.93 | 0.07 | 8% |
| 900 | 6 | 18 | 60% | 1.02 | 0.04 | 4% |
| 1050 | 3 | 9 | 76% | 1.11 | 0.05 | 5% |
| 1200 | 3 | 9 | 72% | 1.06 | 0.04 | 4% |
| 1350 | 2 | 5 | 80% | 1.06 | 0.01 | 1% |
| Cardiac Output (L/min) | | | | | | |
| Rest | 6 | 18 | 9% | 5.79 | 1.54 | 27% |
| 300 | 6 | 18 | 28% | 11.33 | 2.25 | 20% |
| 600 | 6 | 18 | 42% | 13.10 | 2.15 | 16% |
| 900 | 6 | 18 | 60% | 15.96 | 1.42 | 9% |
| 1050 | 3 | 9 | 76% | 18.91 | 1.32 | 7% |
| 1200 | 3 | 9 | 72% | 18.24 | 2.20 | 12% |
| 1350 | 2 | 5 | 80% | 20.32 | 1.82 | 9% |

Table B-IV. (Cont.)

| Work (kgm/min) | Subj. | Tests | % $\dot{V}_{O2}$ max | Mean | SD | coeff. var. |
|---|---|---|---|---|---|---|
| <u>Heart Rate</u> | | | | | | |
| Rest | 6 | 18 | 9% | 74 | 15 | 20% |
| 300 | 6 | 18 | 28% | 93 | 13 | 14% |
| 600 | 6 | 18 | 42% | 114 | 13 | 11% |
| 900 | 6 | 18 | 60% | 139 | 16 | 11% |
| 1050 | 3 | 9 | 76% | 164 | 13 | 8% |
| 1200 | 3 | 9 | 72% | 151 | 9 | 6% |
| 1350 | 2 | 5 | 80% | 163 | 7 | 4% |
| <u>Stroke Volume</u> | | | | | | |
| Rest | 6 | 18 | 9% | 79.9 | 19.7 | 25% |
| 300 | 6 | 18 | 28% | 113.4 | 24.6 | 22% |
| 600 | 6 | 18 | 42% | 115.8 | 18.5 | 16% |
| 900 | 6 | 18 | 60% | 116.2 | 14.6 | 13% |
| 1050 | 3 | 9 | 76% | 115.7 | 11.9 | 10% |
| 1200 | 3 | 9 | 72% | 121.3 | 16.9 | 14% |
| 1350 | 2 | 5 | 80% | 125.0 | 11.0 | 9% |
| <u>Arterio-Venous Oxygen Difference (Vol%)</u> | | | | | | |
| Rest | 6 | 18 | 9% | 5.3 | 1.0 | 19% |
| 300 | 6 | 18 | 28% | 8.5 | 1.5 | 18% |
| 600 | 6 | 18 | 42% | 10.2 | 1.5 | 15% |
| 900 | 6 | 18 | 60% | 12.0 | 1.2 | 10% |
| 1050 | 3 | 9 | 76% | 12.0 | 1.0 | 8% |
| 1200 | 3 | 9 | 72% | 14.0 | 1.5 | 11% |
| 1350 | 2 | 5 | 80% | 14.2 | 1.3 | 9% |

## C. BODY FLUIDS AND ELECTROLYTES UNDER CONDITIONS OF SINGLE AND COMBINED STRESS

Maintenance of homeostasis in the body with regard to fluids and electrolytes in the face of single or multiple stresses deserves serious concern in manned space operations in view of the possible effects of weightlessness on body fluid regulation. It has been postulated that the increase in central blood volume on transition to the gravity-free state induces inhibition both of ADH release through left atrial receptors and of aldosterone production through right atrial receptors. This results in both salt and water diuresis (7 ). While the validity of this hypothesis on the effects of zero-G on body fluids awaits testing by appropriate physiological measurements in actual space flight, precise knowledge of the influence of additional factors such as thermal stress with or without physical activity, which may also be encountered by the astronauts, is imperative in order to properly assess the effects of weightlessness per se.

The following investigations were undertaken to re-evaluate current concepts regarding the effects of heat and exercise on body fluids and electrolytes with particular emphasis on changes in circulating blood volume.

### I. Changes in Blood Volume, Plasma Constituents, and Total Body Fluid in Heat at Rest

In their review of research related to blood volume responses to rest in the heat, Bass and Henschel ( 5 ) concluded that hemodilution is one of the earliest responses of the body fluids to heat stress. Recent support for this view comes from Senay and Christensen (20) who observed hemodilution in men during the first 2-1/2 hours of dehydrating rest in a hot environment (43.3C db, 29C wb). However, most of these studies have relied on estimates of blood volume changes based on changes observed in Hct, plasma protein concentration, or refractive index. Such estimates are based on the assumptions that red blood cell volume remains constant and that plasma proteins neither enter nor leave the vascular system during the course of the experiment. Both of these assumptions are open to debate. Studies which included

blood volume determinations often did so without employing immediate control measurements. Since dye-dilution methods were most often used in these investigations, they were limited to one blood volume determination per day, and therefore had to depend on control measurements made on some previous day. It seems apparent that any definitive study of acute changes in blood volume during exposure to environmental stresses must base its findings on immediate control and immediate post-exposure blood volume determinations.

The time course of plasma volume expansion in response to heat stress is not well defined, although it is said to occur during the first 30 minutes of exposure ( 1, 11 ) and to persist for two to four hours even when water is withheld from the subjects ( 1, 20 ). This initial hemodilution is said to give way to hemoconcentration as a result of dehydration when water is withheld during prolonged heat exposure (1, 3, 11 ). Our earlier work has failed to confirm the persistence of hemodilution for up to four hours of heat exposure. When eight men were exposed to 4-1/2 hours of rest without fluid replacement in environments of 50C db, 25C wb (n = 5) and 43.5C db, 29C wb (n = 3), all showed plasma volume reduction. In these experiments, blood volume was determined by CO immediately before and again during the last minutes of heat exposure. Initial hemodilution was indicated by a slightly decreased hematocrit observed in two of the men during the first two hours of heat exposure. A blood volume determination made on one of the subjects after 90 minutes of exposure revealed a 4% increase in plasma volume and a 2% increase in red blood cell volume. However, all subjects exhibited hemoconcentration at the time of the last blood volume determination in the heat. As average weight loss of about 2.5% was associated with plasma volume reductions averaging about 6.5%.

Blood volume responses to heat exposure while maintaining water and salt balances have also received considerable attention. But again, results are often based on indirect estimates rather than actual blood volume determinations. The purpose of the first part of this investigation was to re-examine and quantitate the alleged expansion of plasma volume in men exposed to heat at rest with fluid replacement, whereby blood volume determinations were made immediately pre- and post-exposure. The selection of a method for blood volume is critical, because it must provide valid results

when repeated on the same day and be independent of changes in plasma protein content. This eliminates the dye-dilution methods, but we have found the CO method to be a good choice.

Procedure:

The subjects for this study were three healthy men, aged 28, 35, and 62. Arriving in the laboratory in the post-absorptive state, the subject was dressed in shorts, fitted with skin and rectal thermocouples, and a flexible teflon catheter was inserted into an antecubital vein. Following 45-60 minutes of rest in the reclining position in a neutral environment (29-30C), the control blood volume was determined by the CO method (15). Overnight urine was collected and the subject was moved to a hot room (50C db, 26C wb) where he reclined on a saran net lounge chair which rested on a platform balance. Body weight was recorded with an accuracy of ± 15 grams at regular intervals during the 4-hour period of rest in the heat. Water and salt losses were replaced at 15 minute intervals with 0.1% saline which was kept at or near body temperature. Blood was drawn for CO, Hct, Hb, plasma electrolytes, and plasma protein determinations after approximately 5, 20, 60, 120, 180, and 215 minutes of heat exposure. Blood volume was determined again during the last minutes of rest in the heat. The subject then left the hot room, urine was collected, and the experiment was terminated.

Results and Discussion:

The results of these experiments are shown in Figs. C-1 through C-4 and in Table C-I. Mean evaporative rates for the men were similar, averaging 253 $g/m^2 \cdot hr$ and total evaporation for the period averaged 1952 grams. Attempts to replace fluid losses with saline at 15 minute intervals met with varied success, and final water deficits were 64, 376, and 534 grams for subjects VR, UL, and JL, respectively. Only JL was unable to comfortably drink saline in volumes which equaled his evaporative rate. Investigator error prevented maintenance of exact water balance for subject UL. Estimations of red cell volume reported from 5 through 215 minutes of heat exposure were based on the assumption that changes in red cell volume for each succeeding sample period could be calculated by averaging the difference between the control and final blood volume determinations with the number of blood samples. Approximately 12 ml of blood were drawn for each sample. As expected, red cell volume changed very slightly during rest in the heat.

The average decrease of 80 ml between control and final blood volume determinations was just about accounted for by the estimated 100 ml of blood drawn during the interim.

During the first hour of heat exposure, weight changes ranged from +18 to -189 grams, and Hct determinations for this period suggested plasma decreases for two of the men and a plasma increase for subject VR. Subsequent Hct determinations during the remaining 3 hours of heat exposure continued to indicate slight plasma volume increases for VR and plasma volume decreases for the other subjects. It may be significant to note that our attempts to replace fluid losses were most successful with subject VR. However, Hct increases were observed in subject UL when water deficit was limited to about 100 grams. These variations in plasma volume response to rest in the heat may also be in part related to individual variability, especially if this variability pertains to heat acclimatization. VR is a native of Bhopal, India; which has a semi-tropical climate. He had been in Albuquerque about two months before participating in these experiments, which were conducted in December. The other subjects were long time residents of Albuquerque, and neither had engaged in activities which could be expected to lead to heat acclimatization.

Rectal temperature increases during the heat exposure were as follows:

| | Rectal Temperature, $^{o}C$ | | |
|---|---|---|---|
| Subj. | Initial | Final | Difference |
| VR | 37.2 | 38.1 | +0.9 |
| UL | 37.6 | 38.1 | +0.5 |
| JL | 36.8 | 37.6 | +0.8 |

The differences in the state of hydration among the subjects in this study were apparently too slight to have greatly affected thermoregulation. In fact, the subject exhibiting the least water deficit (VR) experienced the greatest increase in $T_{RE}$.

Except for subject JL, plasma protein concentration and plasma osmolality generally reflect the trend, if not the magnitude, of hemodilution or hemoconcentration as indicated by Hct. However, the sharp initial drop in JL's plasma osmolality was associated with a similar drop in plasma protein concentration occurring in the presence of an increased Hct. Plasma

$Na^+$ and $Cl^-$ remained relatively constant for all subjects throughout the entire rest in the heat. Initial decreases in average plasma $K^+$ were followed by only slight changes during the remainder of heat exposure. The absence of appreciable changes in the Hb/Hct ratio is an indication of the absence of shrinking or swelling of the red blood cells.

Observations of urine flow and composition are illustrated in Figs. C-3 and C-4. Although attempts were made to replace all water and salt losses as they occurred, all subjects exhibited reduction in urine flow with corresponding increases in specific gravity and osmolality, thus suggesting ADH activity. Aldosterone activity was also indicated by the conservation of $Na^+$ which was evident in its lowered hourly urinary output for all subjects, but urinary excretion of $Cl^-$ and $K^+$ remained less definitive. The variability in the states of hydration of the men during heat exposure may be partially responsible for the variability observed in kidney function.

The results of these experiments provide little support for the generalization that blood volume expands when man is acutely exposed to a hot environment. Even when dehydration was minimized by replacing most of the evaporative weight loss with 0.1% saline, only one of the three subjects exhibited an increased plasma volume, and that was limited to 100 ml or +4%. We contend that the blood volume response to rest in the heat is dependent upon several factors, not the least of which include individual variability, heat acclimatization, and the body's state of hydration.

## II. Changes in Blood Volume, Plasma Constituents, and Total Body Fluids During Exercise in Heat and the Effects of Acclimatization

Blood plasma bears a disproportionately large share of the fluid loss when unacclimatized men are acutely dehydrated by work in the heat ( 1 ). We have since confirmed these findings. When unacclimatized men worked on a motor driven treadmill (5.6 km/hr, level) in the heat (50C db, 26C wb) and dehydrated rapidly by an average of 4% of body weight within two hours, their plasma volume decreased an average of 17% or 2.8 times the percentage reduction in total body water (16). This sharp decrease in plasma volume has been attributed to the inability of body fluids to shift rapidly during conditions of profuse sweating. Our observations of fluid shifts into the vascular compartment of men during the first two to five hours of rest following dehydrating work in the heat gives some support to this hypothesis.

It is well known that man can successfully acclimatize to work in hot environments. This acclimatization is characterized by marked improvement in the regulation of body temperatures and the ability to work in the heat without distress (19). The generally accepted indices of acclimatization to work in the heat are decreased heart rate, decreased skin and rectal temperatures, and increased sweat rate for a given rise in rectal temperature ( 6 ). Taylor, Henschel, and Keys (22) and Bass, et. al. ( 6 ) have suggested that the most important adaptations to work in the heat are those concerned with cardiovascular function. Certainly the maintenance of circulating blood volume is important to thermoregulation. Thus, we were interested in the effect of acclimatization on blood volume changes during dehydrating work in the heat.

Methods and Procedures:

Circulatory and thermoregulatory responses to dehydrating work in the heat (50C db, 26C wb) were studied in eight healthy young men. Pertinent physical and bioclinical characteristics of these subjects are given in Table C-II. The aerobic capacity of each subject was determined using the bicycle ergometer following the method described by Luft, et.al. (12). All subsequent work in the heat was standardized at 30% $\dot{V}_{O2\ max}$. Circulatory and thermoregulatory responses to dehydrating work in the heat were studied in the winter in the unacclimatized subjects. They were then subjected to a laboratory acclimatization period which consisted of riding the bicycle ergometer at the standard work load for 100 minutes daily for nine consecutive days in the same hot environment. Water and electrolyte deficits were replaced during all acclimatization work bouts. The men rested on day 10 and they performed the second dehydrating work experiment on day 11.

Arriving in the laboratory in the post-absorptive state, the subject, dressed in shorts and tennis shoes, was fitted with skin and rectal thermocouples, and a flexible teflon catheter was inserted into an antecubital vein. Following 45-60 minutes of rest in the reclining position, the control blood volume was determined by the CO method as described elsewhere (15). Overnight urine was collected, body weight recorded on a platform balance to within ± 15 grams, and the subject was then moved to the environmental chamber where he worked on a bicycle ergometer without water and salt replacement. Work continued as long as tolerable, but up to a maximum of 120 minutes. Blood samples were drawn for hematocrit, hemoglobin,

plasma electrolytes, plasma osmolality, and plasma proteins after approximately 10, 60, and during the final minutes of work in the heat. After finishing work, the subject was moved to a comfortable room (25C) where he reclined, covered with a light sheet, and rested without food or drink for about four hours. Blood samples were drawn at approximately 10, 30, 60, 120, and 180 minutes, and the final blood volume determination was made after approximately 250 minutes of this resting recovery. All blood samples were drawn from an arm vein without stasis from the indwelling catheter. The microhematocrit method was used for determining venous hematocrit (Hct). No corrections were made for trapped plasma. Hemoglobin (Hb) concentration in the blood was determined by the Drabkin technique (9) using the Beckman DU spectrophotometer calibrated against Hycel's methemoglobin standards. Plasma was analyzed for sodium, potassium, and chloride concentrations on a Technicon Autoanalyzer. Urine and sweat were analyzed for sodium and potassium on an Instrumentation Laboratories, Inc. Flame Photometer, Model 143. Chloride concentrations were determined by a Buchler-Cotlove Chloridometer. Total plasma proteins were determined by the Biuret method, and plasma albumin, $alpha_1$-, $alpha_2$-, beta-, and gamma-globulin were analyzed by electrophoresis. Plasma and urine osmolality were determined on an Advanced Instruments Osmometer, Model 64-31. Body density, percent body fat, and lean body mass (LBM) were estimated by hydrostatic weighing as described by Luft and Lim (13). Total body water (TBW) was estimated as 73.2% of LBM according to Pace and Rathbun (17). Sweat samples were obtained by means of an elbow length industrial rubber glove, covered with a wet terry cloth, from 45 to 60 minutes of the work in the heat. Skin temperatures were recorded at frequent intervals with an Elektrolaboratoriet (Copenhagen) electric universal thermometer, type TE3. Rectal temperature was monitored by a Yellow Springs thermometer. Air movement in the room was maintained at 10-11 ft/sec. Metabolic weight loss amounted to less than 2% of the total weight loss during the dehydrating work in the heat, and was therefore disregarded. Heart rate (ECG) was recorded at regular intervals on a Hewlet-Packard Electrocardiograph.

Results and Discussion:

The effects of acclimatization on work tolerance, evaporative rate, sweat electrolytes, rectal temperature, and heart rate observed in eight

men working in a hot environment without fluid replacement are given in Figs. C-5 and C-6 and in Tables C-III through C-VII. The improved ability of the men to perform dehydrating work in the heat as a result of the acclimatization regimen is apparent. The differences observed in work time, evaporative rate, sweat $Cl^-$, and 60-minute rectal temperature and heart rate as a result of acclimatization were significant ($p < 0.05$). Although none of the unacclimatized men were able to complete two hours of work in the heat without developing signs of circulatory embarrassment, six of the eight acclimatized subjects completed the two hours of dehydrating work without significant distress. One of the men, DS, showed no improvement in work tolerance in the heat as a result of acclimatization.

Average weight loss and changes in Hct and estimated plasma volume are presented in Fig. C-7 and in Tables C-VIII through C-XII. The rate of weight loss (evaporative rate) for the acclimatized men was parallel with but slightly greater than that observed before acclimatization. There appeared to be no change in the evaporative rate as dehydration progressed throughout the work in the heat. Plasma volume was estimated from Hct and the control red cell volume, with appropriate corrections for the volume of red cells lost during blood sampling. The differences between the control and the final red cell volumes, both before and after acclimatization, were not significant. The rate of plasma volume decrease appeared to occur in two stages during the first hour of dehydrating work in the heat. The first stage was exhibited by a very rapid rate of decrease observed during the first 10-20 minutes. This was followed by a continued, but slower rate of decrease through the first hour of dehydrating work in the heat. The unacclimatized men showed no departure from this second stage as work and dehydration continued from 60 through 77 minutes when they were no longer able to continue. However, after acclimatization the men exhibited a third stage of plasma volume decrease which occurred between 60 and 112 minutes of work. Although the evaporative rate appeared to continue unaffected by progressive dehydration, the rate of plasma volume decrease during this period was less than during the preceding hour. However, the statistical significance of this change remains to be tested. It seems probable that the initial stage of hemoconcentration was the result of both the change in activity and the imposed thermal stress. The slower continued decrease in

plasma volume as dehydrating work continued was probably closely associated with the rate of dehydration. A comparison of plasma volume decrease relative to total body water decrease and to the increase in plasma protein concentration (PPconc) as a result of dehydrating work in the heat, before and after acclimatization, follows:

| | ① %ΔTBW | ② %ΔPlasma | ② ÷ ① | ③ %ΔPPconc |
|---|---|---|---|---|
| Unaccl. | -3.23 ± 1.06 | -15.5 ± 5.6 | 4.80 | +17.2 ± 4.2 |
| Accl. | -4.91 ± 1.22 | -16.5 ± 3.2 | 3.36 | +19.0 ± 7.0 |

Thus, in these experiments the unacclimatized men finished work with a percentage decrease in plasma volume which was 4.8 times greater than that of total body water whereas it was only 3.36 times greater after acclimatization. The ability of the circulatory system to maintain plasma volume in the face of acute dehydration had improved about 30%. As we have reported earlier (16), during the first 30-60 minutes of resting recovery the plasma volume regained about half of the deficit incurred during the dehydrating work in the heat. The slow rate of plasma volume decrease observed from one to four hours of this resting recovery is probably attributed to a slight but progressive dehydration as the men were given neither food nor drink during this period.

Plasma electrolyte concentrations are presented in Fig. C-8 and in Tables C-IX and C-X. The increases in plasma $Na^+$ and $Cl^-$ during the dehydrating work in the heat were significantly greater ($p < 0.01$) than the respective control values, both before and after acclimatization. The plasma remained concentrated with respect to these electrolytes through the four hour resting recovery. Water loss via hypotonic sweat can be expected to cause an increase in plasma electrolyte concentration. The fluid returning to the circulation during the resting recovery must have been about isotonic with the plasma because, although the plasma volume was increased about 300 ml during the first hour of this period, changes in plasma $Na^+$ and $Cl^-$ were slight. Plasma $K^+$ increased during the dehydrating work and decreased during the resting recovery, but these changes were not significant ($p > 0.05$).

Observations of plasma protein concentrations, plasma osmolality, and calculated Hb/Hct ratio are presented in Figs. C-9 and C-10 and in Tables

C-IX and C-X. The changes in plasma volume during the dehydrating work and also during the resting recovery period are well reflected by changes in plasma protein concentration. The alleged net gain or loss of plasma proteins during dehydrating work and heat stress reported by Senay and Christensen (21) is not supported by our data:

| | Plasma Protein (total grams) | |
|---|---|---|
| n = 8 | Unacclimatized | Acclimatized |
| Control | 226 | 226 |
| Final minutes of work in the heat | 224 | 223 |
| At the end of recovery period | 218 | 224 |

However, the general fluctuations observed in plasma protein fractions $alpha_1$-, $alpha_2$-, beta-, and gamma-globulin during dehydrating work in the heat are in agreement with these authors.

The acclimatized subjects exhibited a greater increase in plasma osmolality during the dehydrating work. This was undoubtedly one of the factors responsible for their improved ability to retain plasma water during dehydration. The Hb/Hct ratio provides a crude index of red cell swelling or shrinking. The sharply increased ratio during dehydrating work in the heat and the decrease observed during the resting recovery suggests respective loss and gain of water by the red blood cell. This red cell shrinkage during dehydrating work in the heat appeared to occur at a much faster rate before acclimatization.

Changes in urine components as a result of the dehydrating work and heat stresses, both in the unacclimatized and in the acclimatized subjects, are presented in Figs. C-11 and C-12 and in Tables C-XIII and C-XIV. The effects of ADH and aldosterone activity are manifested in the sharp reductions in urine flow and sodium excretion, respectively. Other obvious effects of dehydrating work were increases in urine specific gravity and osmolality. Changes in urine pH and in potassium excretion appeared to be little affected by the imposed dehydration, work, and heat stresses.

Summary and Conclusions:

Changes in blood volume, plasma constituents, and total body fluids were studied in men acutely exposed to rest or work in the heat (50C db,

26C wb). In the rest experiments, blood volume was determined in three men by CO immediately before and during the last minutes of four hours of heat exposure. Water and electrolyte losses were replaced at 15-minute intervals with 0.1% saline kept at or near body temperature. Total evaporation for the period averaged 1952 grams, and final water deficits ranged from 64 to 534 grams. Even with water and salt replacement, renal conservation of water and sodium was evident. Red blood cell volume remained constant. Only one of the subjects exhibited an increased plasma volume and that was limited to 100 ml or +4%. These data do not support the generalization that plasma volume expands when man is exposed to rest in a hot environment. We conclude that circulatory responses to heat are individual characteristics which are dependent upon several factors including heat acclimatization and the body's state of hydration.

In the dehydrating work in the heat experiments, eight unacclimatized men worked an average of 77 minutes and dehydrated an average of 2% of body weight. Red blood cell volume did not change, but plasma volume decreased an average of 15.5% which was 4.8 times greater than the percentage decrease in total body water. Within 30 to 60 minutes after leaving the heat the plasma regained about half of the volume lost during the dehydrating work. No further shift of fluid into the plasma was observed after the first hour of this resting recovery. Following an acclimatization regimen, the ability of the men to perform dehydrating work in the heat was evidently much improved. They worked an average of 112 minutes, with lower heart rates and rectal temperatures, and dehydrated an average of 3% of body weight. Red cell volume remained constant, but plasma volume decreased an average of 16.5% which was 3.4 times greater than the percentage decrease in total body water. Again, half of this plasma loss was replaced during the first hour of continued dehydration while resting in a comfortable room following work in the heat. Although plasma protein fractions fluctuated widely during and following the work in the heat, there was no net gain or loss of total plasma protein in either the unacclimatized or the acclimatized men. ADH and aldosterone activity were evidenced by marked renal conservation of water and sodium, respectively.

Plasma loses a disproportionately large amount of water during acute dehydration by work in the heat in the acclimatized as well as the unacclimatized

man. However, the acclimatized men did improve 30% in their ability to maintain plasma volume in the face of acute dehydration. This must be one of the factors responsible for the improved circulatory stability and thermoregulatory responses observed in the acclimatized men in this study. The shift of fluid into the plasma compartment during the resting recovery has significant practical application. It is suggested that circulatory embarrassment may be greatly delayed if frequent rest intervals are interspersed with work when man is faced with the combined stresses of dehydration and work in hot environments.

# Comparison of Manometric and Infrared Methods for Determining Carbon Monoxide in Blood

**Loren G. Myhre**

Twelve samples of blood containing carbon monoxide (CO) ranging from 0.24 to 6.80 vol % were analyzed in duplicate by a manometric method and by two other methods in which an infrared CO meter is used. The analytical precision was within ±0.015 vol % for all methods, and the differences observed in blood CO between any two methods were not statistically significant. One of the methods with the infrared CO meter was preferred because, without sacrificing either precision or accuracy, it was considerably more convenient and technically less demanding than either of the other methods.

The use of carbon monoxide (CO) for determining blood volume is often rejected because of the difficulties inherent in the methods for the precise analysis of CO in blood. Our modification (*1*) of the Horvath and Roughton (*2*) manometric method for determination of blood CO was an attempt to make this technique more applicable to routine laboratory use. With a precision of ±0.02 vol % this method proved to be satisfactory for determining blood volume by CO, but the procedure remained technically difficult and time-consuming.

The development of equally precise but much more convenient methods by Gaensler et al. (*3*) and Coburn et al. (*4*) have presented attractive alternatives. These methods will be referred to subsequently as the Gaensler method and the Coburn method, respectively. These investigators described different techniques, based on the method of Lawther and Apthorp (*5*), for extracting CO from blood for infrared analysis. Unfortunately, Coburn limited his analyses to blood CO concentrations ranging from 0.1 to 1.0 vol %, which is considerably below that found in most samples when determining blood volume by CO. Although the precision of the method described by Gaensler seemed to be consistent for blood CO ranging from 0.11 to 4.41 vol %, his comparison of it with the method of Van Slyke and associates (*6*) was discouraging because of the large variability found in the blank corrections for the latter method.

The purpose of this study was to compare the above three methods for determining blood carbon monoxide. Particular emphasis was placed on selecting blood CO concentrations that were within the range observed in determination of blood volume by CO.

## Materials and Methods

For each comparison, 30 ml of blood was exposed to 0.3% CO in air flowing through a rotating 250-ml tonometer. The exposure time was varied to provide blood CO concentrations ranging from about 0.4 to 6.8 vol %. The blood was stored in a gas-tight syringe and kept at 8°C until analyzed in duplicate by each of the methods studied. This was usually completed within 36 h after withdrawing blood from the tonometer. A 2-ml blood sample was used for all analyses.

The manometric method used for determining blood CO was our modification of the method described by Horvath and Roughton. We have further modified this technique by increasing the concentration of the KOH from 1.0 to 2.0 mol/liter. This change eliminated a "boiling" effect often produced by the more dilute alkali solution. The correction factor used in this technique was determined by averaging several blank determinations before beginning each day's determinations.

The principle of the methods is the same; any CO bound to hemoglobin is liberated by oxidizing the heme ferrous ion to ferric ion. The method of Gaen-

From the Department of Physiology, Lovelace Foundation for Medical Research, 5200 Gibson Blvd., S.E., Albuquerque, N. Mex. 87108.

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sler extracts the CO under reduced pressure in a Van Slyke apparatus. In the Coburn method CO is extracted by bubbling $O_2$ through the methemoglobin solution into a collecting tonometer. In both methods, the extracted gas is analyzed for CO in an infrared analyzer (Model 15A, Beckman Instruments, Inc., Fullerton, Calif. 92634). The infrared CO analyzer was calibrated against known concentrations of CO that were prepared by diluting CO (C. P. grade, 99.5%) trapped in a stopcock bore of measured volume with air free of CO and $CO_2$.

## Results and Discussion

Table 1 shows the results of 12 duplicate determinations of each of the three different methods on the same blood sample. The analytical precision of the analyses was similar with duplicate determinations averaging within +0.02 vol % for all methods. When comparing the concentration of blood CO obtained by the different methods for the same blood sample, the manometric method gave values averaging 1.47 and 1.16% greater than those obtained by the Gaensler and the Coburn methods, respectively. The differences obtained in these comparisons were not statistically significant (*t* test), and their magnitude appeared to be unrelated to the blood CO concentrations for values ranging from 0.24 to 6.80 vol %. In brief, each of the three methods studied yielded essentially the same values for blood CO and they did this with equal precision in our hands. However, we found the Coburn method to be considerably more convenient and technically less demanding. Although the analytical time was similar, about 20 min per analysis for all methods, the time involved in preparing the extraction chambers for succeeding analyses was considerably less for the Coburn method. The coagulum clinging to the Van Slyke extraction chamber is difficult to remove; on the other hand, the reaction chamber used in the Coburn method may be brushed clean in a few seconds.

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Table I. Comparisons of Three Methods for Determining Blood Carbon Monoxide

| | Manometric | | Gaensler Method | | Coburn Method | | | Percent Difference (C = Coburn, M = Manometric, G = Gaensler) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Sample No. | vol% | mean | vol% | mean | vol% | mean | | $\frac{C-M}{M} \cdot 100$ | $\frac{C-M}{M} \cdot 100$ | $\frac{G-C}{M} \cdot 100$ |
| 1 | 0.244<br>0.244 | 0.24 | 0.240<br>0.246 | 0.24 | 0.240<br>0.240 | 0.24 | | 0.0 | 0.0 | 0.0 |
| 2 | 0.463<br>0.440 | 0.45 | 0.404<br>0.404 | 0.40 | 0.419<br>0.414 | 0.42 | | -11.1 | -6.7 | -4.8 |
| 3 | 0.974<br>0.961 | 0.97 | 0.971<br>0.956 | 0.96 | 0.963<br>0.963 | 0.96 | | -1.0 | -1.0 | 0.0 |
| 4 | 1.073<br>1.073 | 1.07 | 1.086<br>1.096 | 1.09 | 1.076<br>1.086 | 1.08 | | 1.9 | 0.9 | 0.9 |
| 5 | 1.889<br>1.886 | 1.89 | 1.864<br>1.854 | 1.86 | 1.864<br>1.844 | 1.85 | | -1.6 | -2.1 | 0.5 |
| 6 | 1.928<br>1.914 | 1.92 | 1.878<br>1.878 | 1.88 | 1.878<br>1.858 | 1.87 | | -2.1 | -2.6 | -0.5 |
| 7 | 2.637[a]<br>2.657 | 2.65 | 2.584<br>2.623 | 2.60 | 2.610<br>2.598 | 2.60 | | -1.9 | -1.9 | 0.0 |
| 8 | 3.041<br>3.029 | 3.04 | 3.086<br>3.086 | 3.09 | 3.081<br>3.088 | 3.08 | | 1.6 | 1.3 | 0.3 |
| 9 | 3.724<br>3.681 | 3.70 | 3.657<br>3.686 | 3.67 | 3.694<br>3.720 | 3.71 | | -0.8 | 0.3 | -1.1 |
| 10 | 4.199[a]<br>4.216 | 4.21 | 4.228<br>4.223 | 4.23 | 4.179<br>4.154 | 4.17 | | 0.5 | 1.0 | 1.4 |
| 11 | 4.921[a]<br>4.933 | 4.93 | 4.808<br>4.802 | 4.81 | 4.845[a]<br>4.874 | 4.86 | | -2.4 | -1.4 | -1.0 |
| 12 | 6.781[a]<br>6.815 | 6.80 | 6.772<br>6.737 | 6.75 | 6.818<br>6.821 | 6.82 | | -0.7 | -0.3 | -1.0 |
| Mean | 2.655 | | 2.632 | | 2.639 | | | -1.47 | -1.16 | -0.36 |
| SD | 0.013 | | 0.011 | | 0.010 | | | 0.33 | 0.21 | 0.16 |
| CV,[b]% | 0.5 | | 0.4 | | 0.4 | | SE | 0.10 | 0.06 | 0.05 |
| | | | | | | | Diff | NS[c] | NS[c] | NS[c] |

[a] A third determination was required to obtain check values which agree within ±0.04 vol%.

[b] CV: *Coefficient of Variation.*

[c] NS - not significant at 0.05 level.

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Appendix C-2

ELIMINATION OF CO BY RESTING ADULT MEN

The applicability of the carbon monoxide (CO) method for repeated blood volume determinations is limited by the rate of carboxyhemoglobin (COHb) elimination between measurements. Allen and Allard ( 2 ) reported that symptoms of CO poisoning consistently begin to appear when the COHb level reaches 15%. Thus, if for no other reason than subject comfort and morale, it is essential that the volume of CO used for blood volume determinations be small enough, and the interim between determinations long enough, to prevent COHb from reaching 15%. To comply with these requirements, the volume of CO administered was markedly reduced from about 133 ml STPD used in our earlier studies with this method (15) to about 56 ml STPD for the present study. As the CO dose becomes smaller, the necessity of precision in blood CO analyses becomes more critical. Our search began for an analytical technique which would be more rapid and less demanding than our modification (15) of the Horvath and Roughton (10) manometric method without sacrificing any of its precision. Our success with the infrared method of Coburn ( 8 ) has already been published (see Appendix C-1).

The precision and convenience of the Coburn method has enabled us to not only obtain reliable blood volume measurements with the administration of smaller volumes of CO, but it has also made it practical for us to follow the rate of COHb elimination between blood volume determinations. We were also interested in establishing the average % COHb found in healthy, non-smoking adult men at rest and post-absorptive. These data are given in Table C-XV along with resting control values for hemoglobin concentration (Hb), venous hematocrit (Hct), and the hemoglobin:hematocrit ratio (Hb/Hct). All subjects were residents of Albuquerque (5350 ft., B = 630 mm Hg). Blood samples were drawn without stasis following 60 minutes of rest with the subjects in the post-absorptive state. Baseline values for carboxyhemoglobin averaged around 1%, and values for Hb, Hct, and Hb/Hct were all slightly higher than published norms for young men at sea level.

The time course for the elimination of CO from the blood of men at rest and breathing room air ($P_{IO_2}$ = 122 mm Hg) is presented in Table C-XVI and in Figure C-13. The elimination of CO from the blood appears to occur

in two phases. Phase one exhibits a relatively rapid rate of CO removal, but it is limited to about the first 20 minutes of air breathing following CO exposure. The second phase exhibits a steady exponential decay continuing for several hours. It is well known that the rate of CO elimination varies inversely with the $O_2$ partial pressure in the inspired air. The results of this study suggest that the half-life of COHb is 5-1/2 hours for healthy young men at rest and breathing room air (B = 630 mm Hg, $P_{IO_2}$ = 122 mm Hg). All three of the subjects studied followed this exponential decay with good agreement. This is in contrast with some reports in the literature giving the half-life of COHb in the blood ranging from 1-1/2 to more than 6 hours ( 4, 18 ) for resting men breathing air. The reason for the great variability in CO elimination under the same resting conditions as reported by these authors remains obscure.

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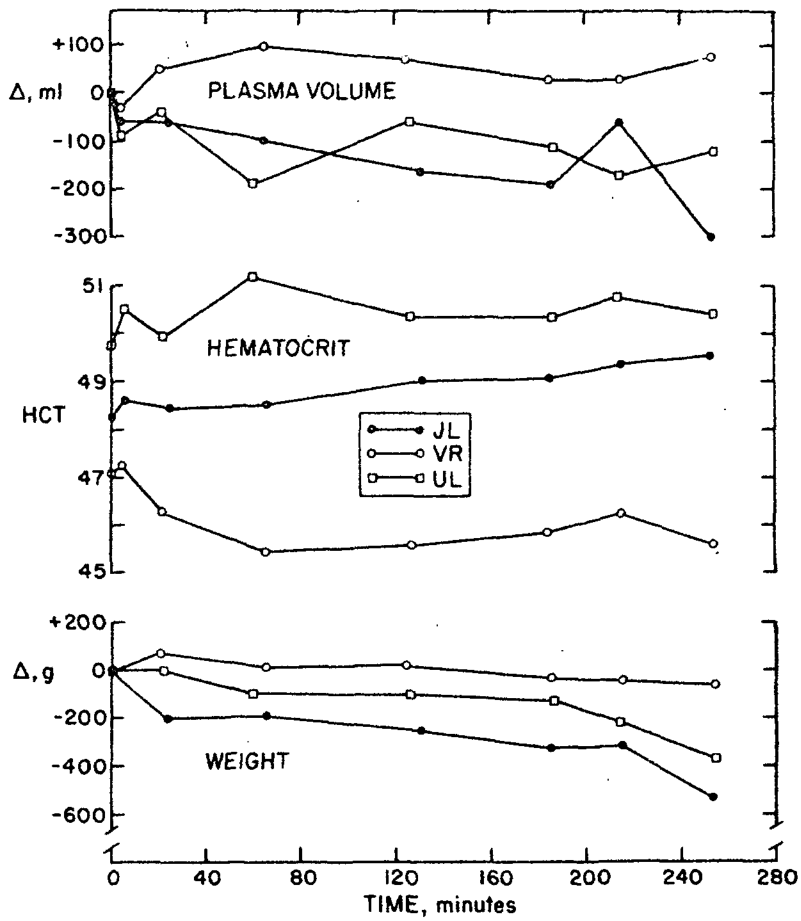


Fig. C-1. Measures of venous hematocrit and changes in body weight and estimated plasma volume observed in three men at frequent intervals during four hours of rest in the heat (50C db, 26C wb) with fluid and salt replacement

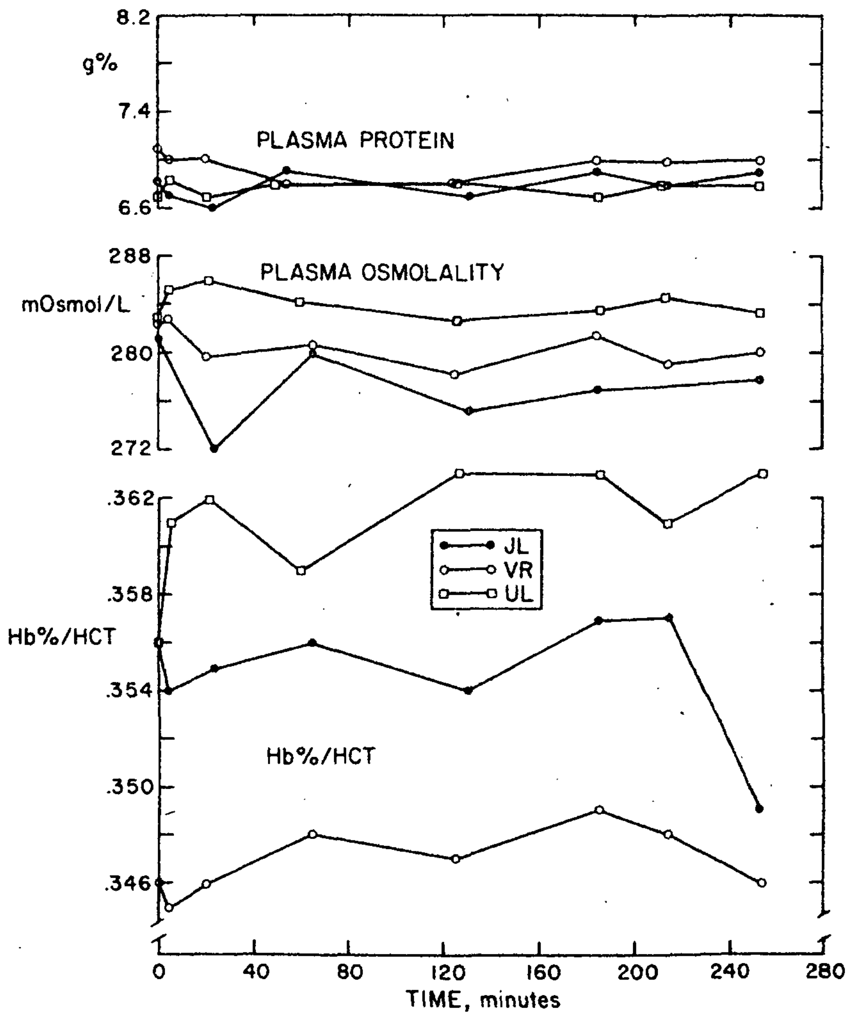


Fig. C-2. Measures of plasma protein concentration, plasma osmolality, and hemoglobin/hematocrit ratio observed in three men before and at frequent intervals during four hours of rest in the heat (50C db, 26C wb) with fluid and salt replacement

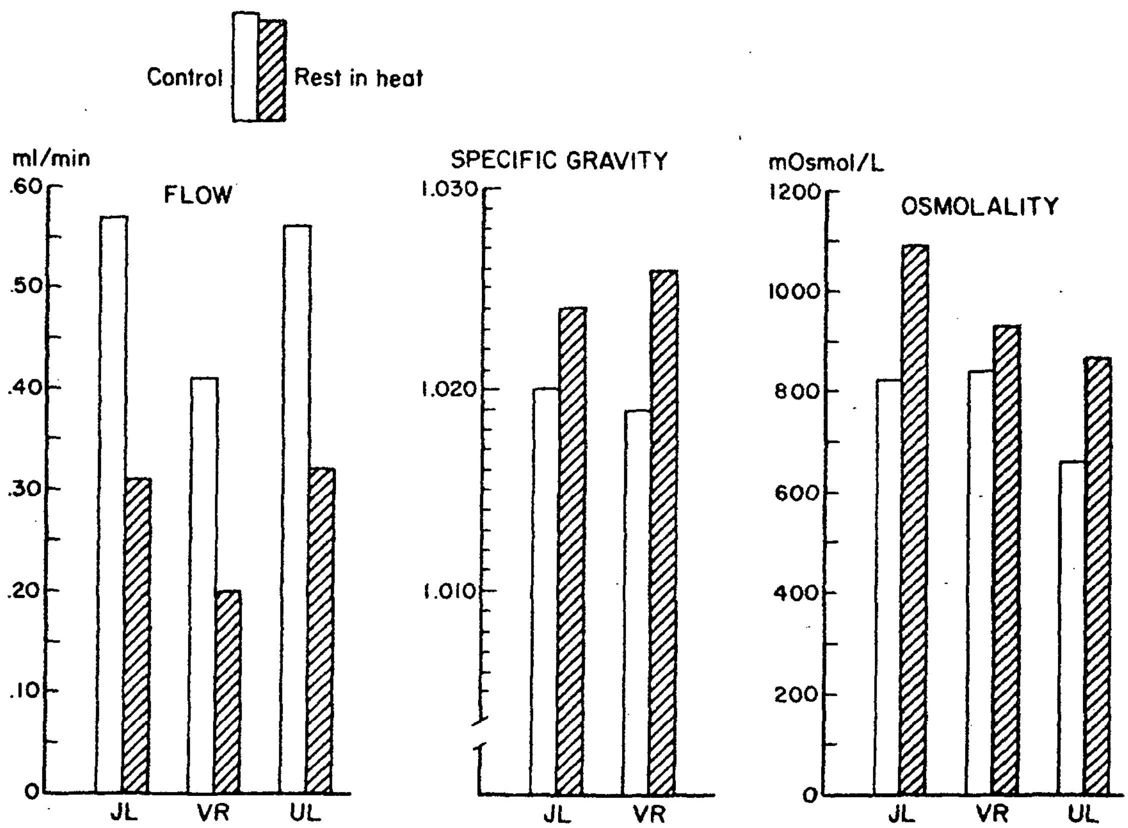


Fig. C-3. Urine flow, specific gravity, and osmolality observed in three men during the post-absorptive control state and again following four hours of rest in the heat (50C db, 26C wb) with water and salt replacement

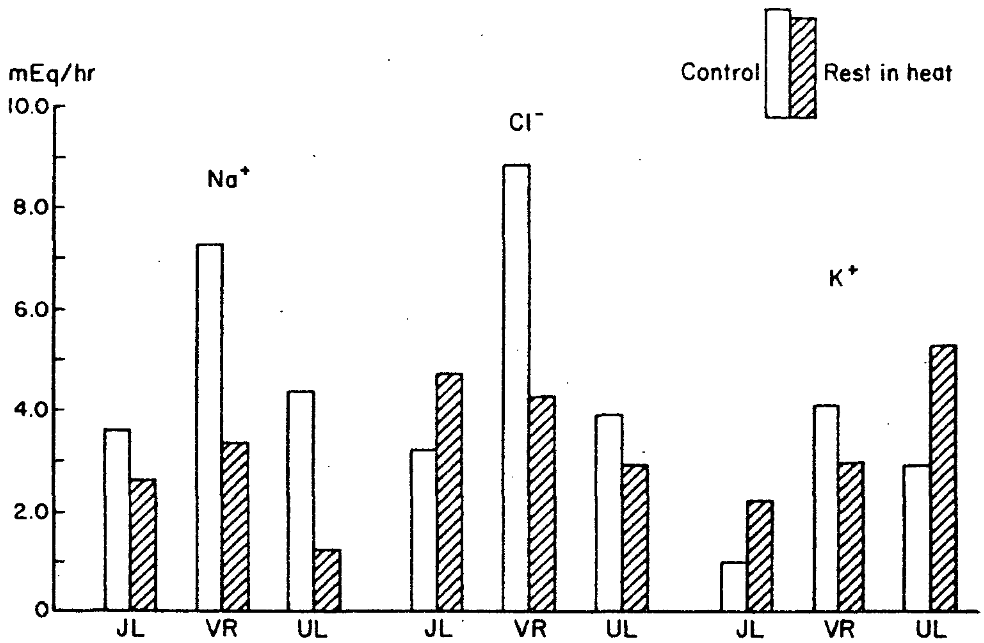


Fig. C-4. Urine electrolyte excretion observed in three men during the post-absorptive control state and again following four hours of rest in the heat (50C db, 26C wb) with water and salt replacement

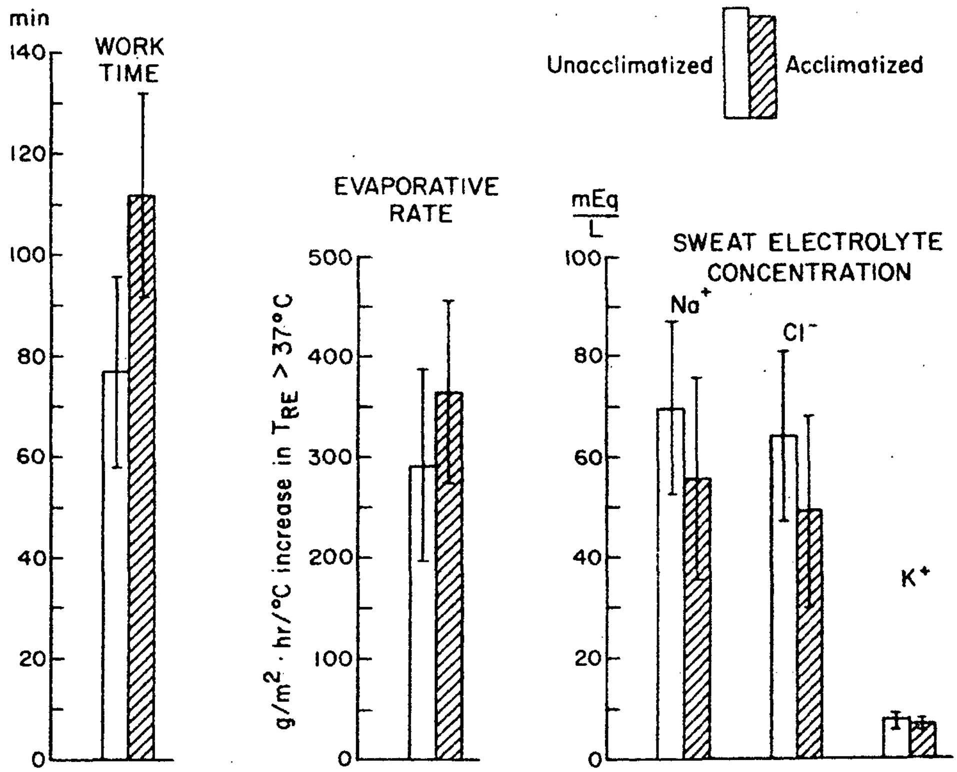


Fig. C-5. Mean and standard deviation values for work duration, evaporative rate, and sweat electrolyte concentrations observed in eight men dehydrating while working in the heat, before and after acclimatization

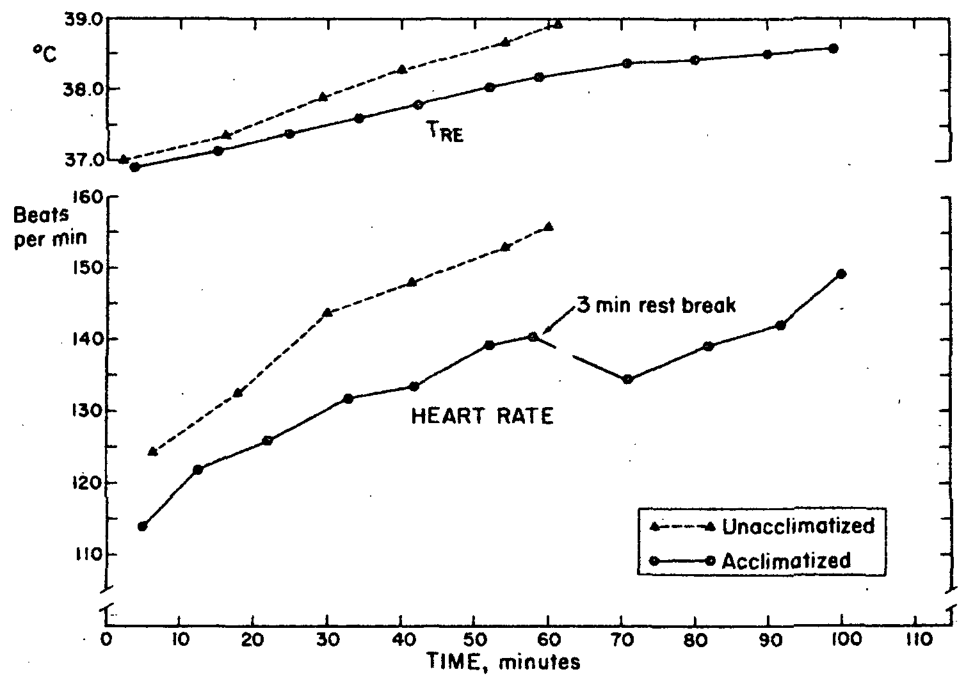


Fig. C-6. Mean heart rate and rectal temperature of six men during dehydrating work in the heat, before and after acclimatization

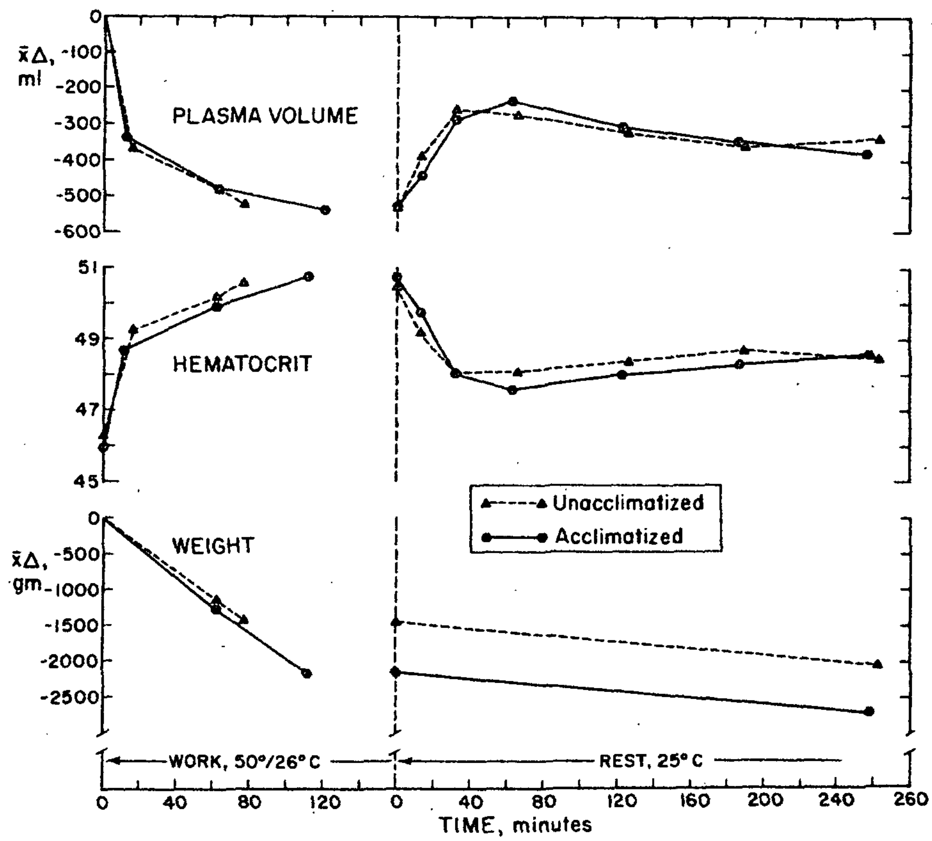


Fig. C-7. Mean values for venous hematocrit and changes in body weight and estimated plasma volume observed in eight men during and following a bout of dehydrating work in the heat, before and after acclimatization

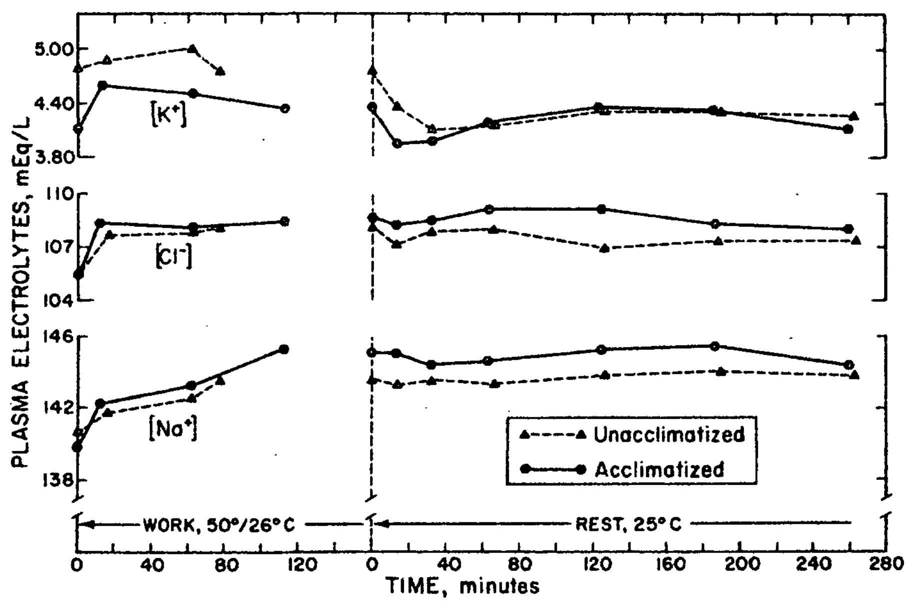


Fig. C-8. Mean values for plasma electrolyte concentrations observed in eight men immediately before and at intervals during and following a bout of dehydrating work in the heat, before and after acclimatization

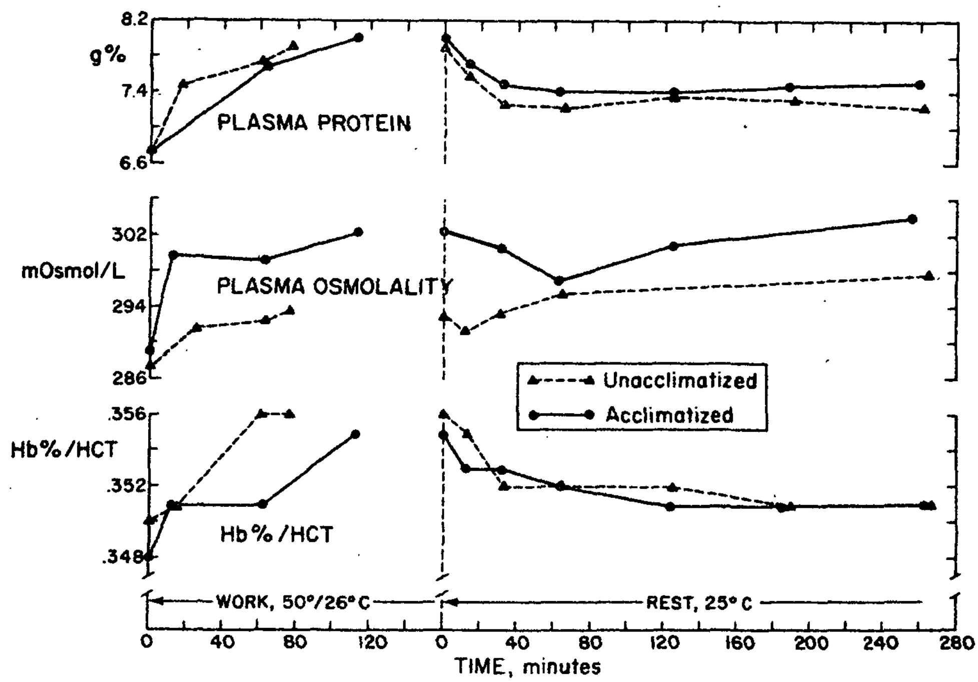


Fig. C-9. Mean values for plasma protein concentration, plasma osmolality, and hemoglobin/hematocrit ratio observed in eight men immediately before and at frequent intervals during and following a bout of dehydrating work in the heat, before and after acclimatization

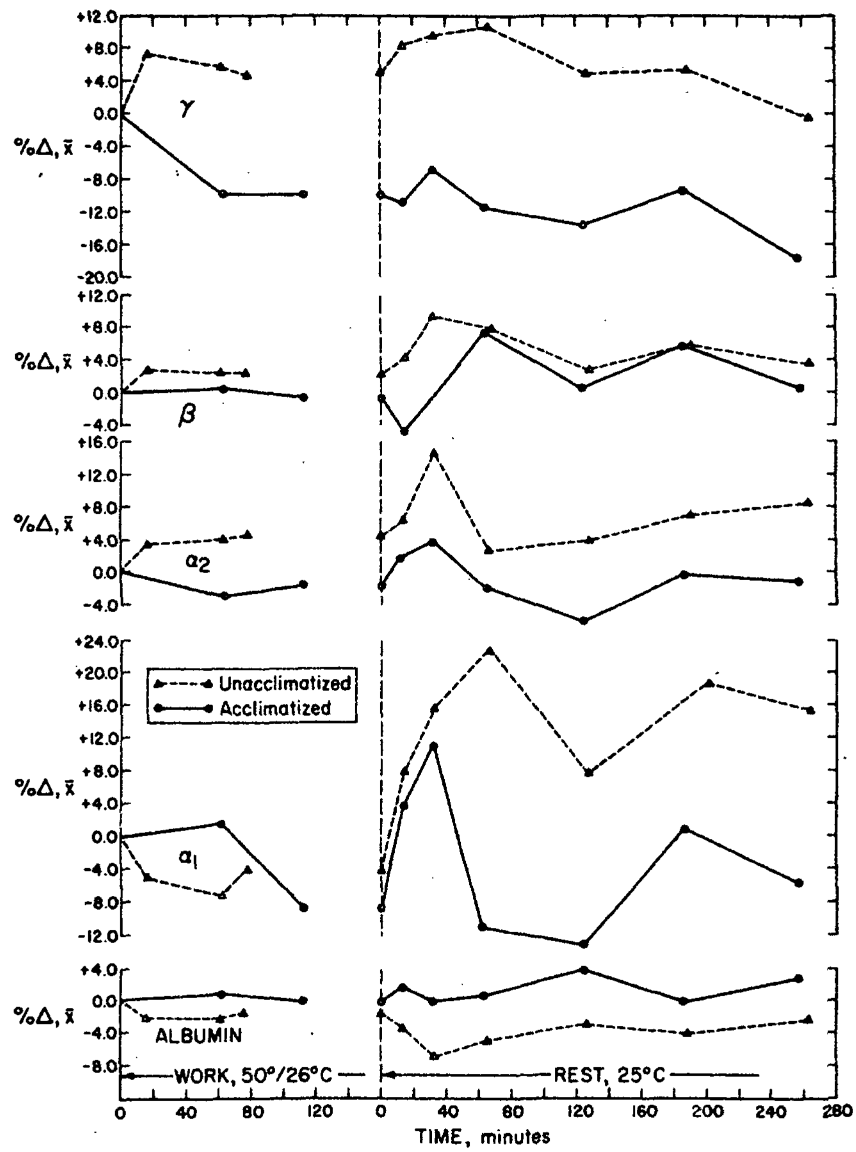


Fig. C-10. Mean values for percent change in plasma protein fractions observed in men at intervals during and following a bout of dehydrating work in the heat, before (n = 8) and again after (n = 6) acclimatization

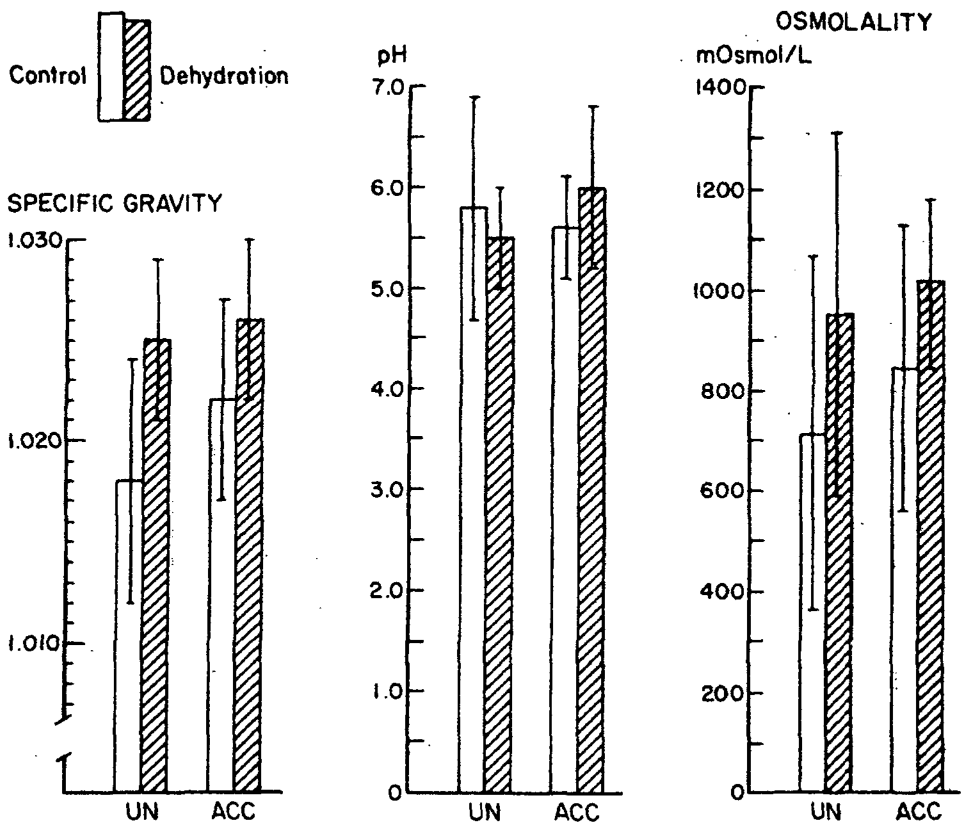


Fig. C-11. Mean and standard deviation values of urine specific gravity, pH, and osmolality observed in eight men during the post-absorptive control state and again following a bout of dehydrating work in the heat (50C db, 26C wb), before (UN) and after (ACC) acclimatization

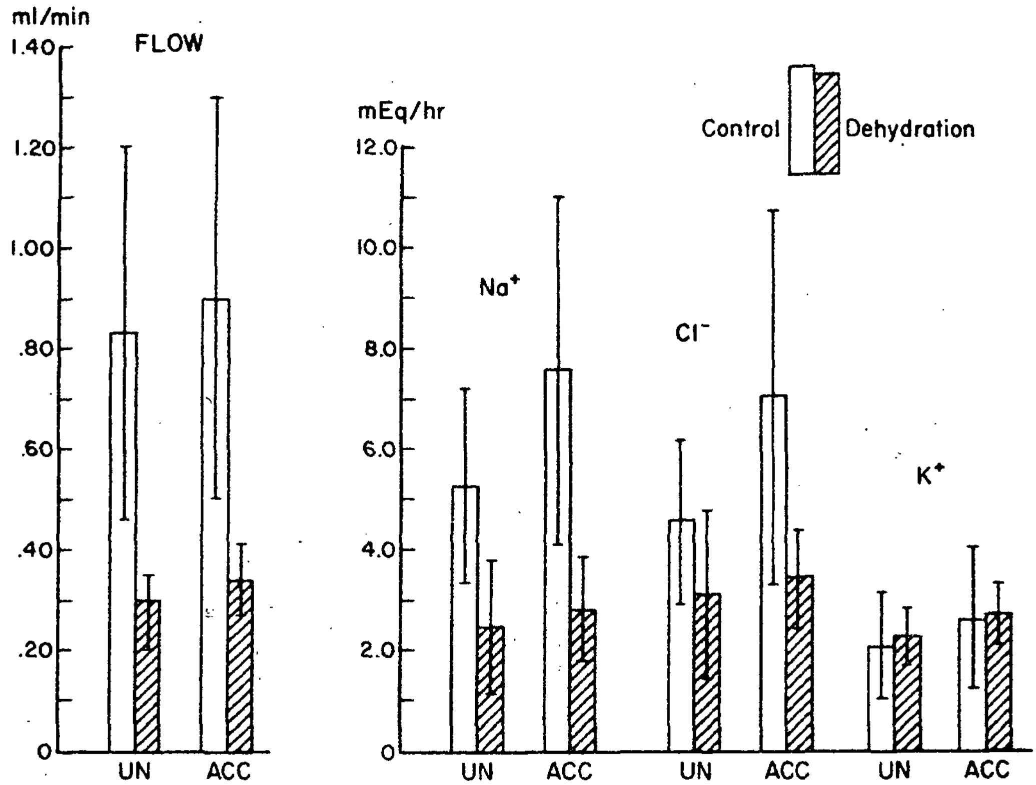


Fig. C-12. Mean and standard deviation values of urine flow and electrolyte excretion observed in eight men during the post-absorptive control state and again following a bout of dehydrating work in the heat (50C db, 26C wb), before (UN) and after (ACC) acclimatization

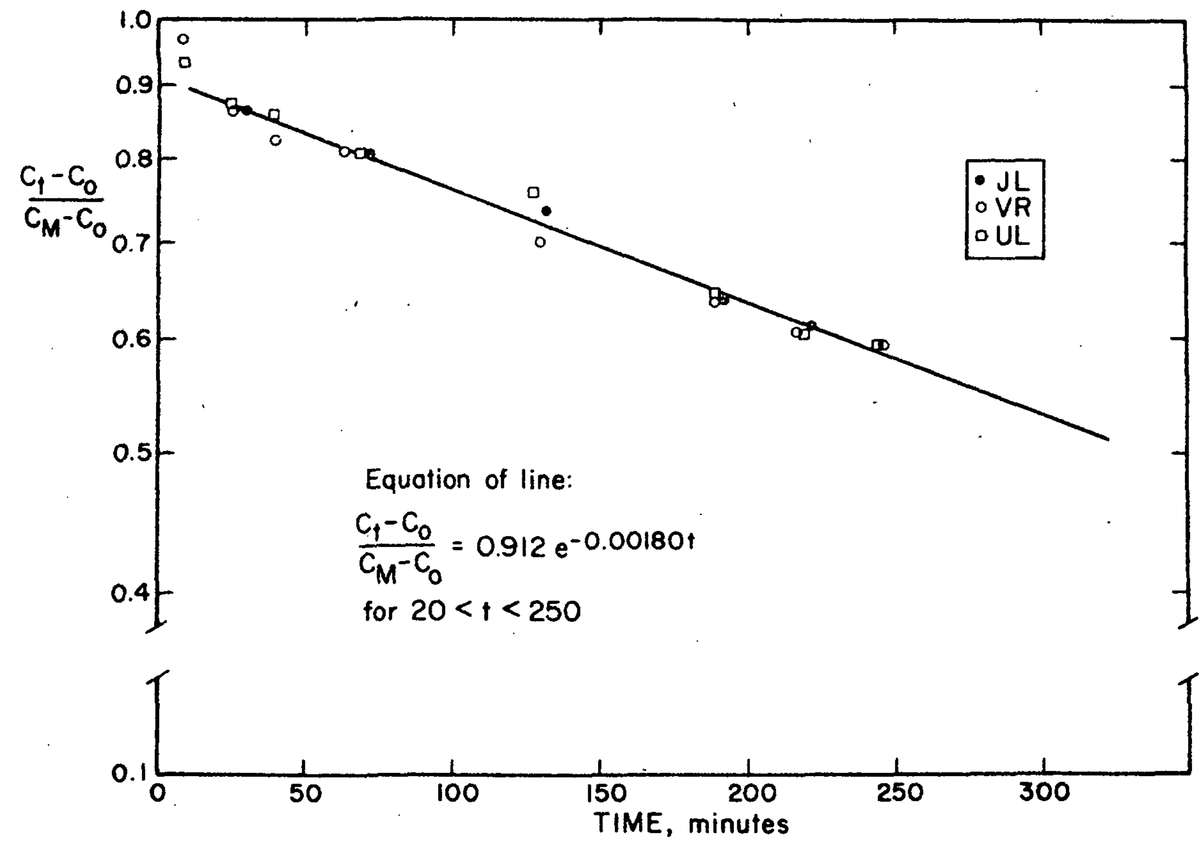


Fig. C-13. Exponential decay for COHb fraction in three men at rest and breathing room air in a hot environment (50C db, 26C wb)

Table C-I. Mean evaporative rate and changes observed in body weight, blood volume, and other blood constituents in three men during rest in the heat (50C db, 26C wb) with fluid and salt replacement

| Subj. | Sample Time (min) | Mean Evap. Rate ($g/m^2 \cdot hr$) | ΔWt. (g) | Blood Volume Plasma | Blood Volume Red Cells | Hb (g%) | Hct | Plasma Prot. (g) | Plasma Electrolytes $Na^+$ | Plasma Electrolytes $Cl^-$ | Plasma Electrolytes $K^+$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| JL | Control | | | 3340 | 2720 | 17.2 | 48.25 | 6.8 | 139 | 104 | 6.2 |
| VR | Control | | | 2260 | 1760 | 16.3 | 47.06 | 7.1 | 140 | 104 | 4.1 |
| UL | Control | | | 3160 | 2720 | 17.7 | 49.73 | 6.7 | 139 | 102 | 6.7 |
| Mean | Control | | | 2920 | 2400 | 17.1 | 48.35 | 6.9 | 139 | 103 | 5.7 |
| JL | 5 | | | 3280 | 2700 | 17.2 | 48.62 | 6.7 | | | |
| VR | 5 | | | 2230 | 1750 | 16.3 | 47.26 | 7.0 | | | |
| UL | 5 | | | 3070 | 2710 | 18.2 | 50.47 | 6.8 | | | |
| Mean | 5 | | | 2860 | 2390 | 17.2 | 48.78 | 6.8 | | | |
| JL | 24 | | -203 | 3280 | 2690 | 17.2 | 48.44 | 6.6 | 139 | 106 | 5.6 |
| VR | 21 | | + 77 | 2310 | 1740 | 16.0 | 46.23 | 7.1 | 139 | 105 | 4.0 |
| UL | 22 | | + 5 | 3120 | 2710 | 18.1 | 49.96 | 6.7 | 139 | 104 | 3.9 |
| Mean | 22 | | - 40 | 2900 | 2380 | 17.1 | 48.21 | 6.8 | 139 | 105 | 4.5 |
| JL | 65 | | -189 | 3240 | 2680 | 17.3 | 48.64 | 6.9 | 140 | 106 | 5.3 |
| VR | 65 | | + 18 | 2360 | 1720 | 15.8 | 45.44 | 6.8 | 139 | 107 | 3.7 |
| UL | 60 | | - 86 | 2970 | 2700 | 18.4 | 51.19 | 6.8 | 140 | 107 | 4.0 |
| Mean | 63 | | - 86 | 2860 | 2370 | 17.2 | 48.42 | 6.8 | 140 | 107 | 4.3 |
| JL | 131 | | -253 | 3180 | 2660 | 17.3 | 49.02 | 6.7 | 140 | 106 | 4.9 |
| VR | 125 | | + 22 | 2330 | 1720 | 15.8 | 45.57 | 6.8 | 139 | 104 | 4.1 |
| UL | 126 | | -104 | 3050 | 2690 | 18.3 | 50.42 | 6.8 | 139 | 104 | 4.1 |
| Mean | 127 | | -112 | 2850 | 2360 | 17.1 | 48.34 | 6.8 | 139 | 105 | 4.4 |
| JL | 185 | | -321 | 3150 | 2650 | 17.5 | 49.11 | 6.9 | 138 | 104 | 5.2 |
| VR | 185 | | - 32 | 2290 | 1710 | 16.0 | 45.86 | 7.0 | 139 | 104 | 3.7 |
| UL | 186 | | -131 | 3050 | 2680 | 18.3 | 50.37 | 6.7 | 137 | 103 | 4.0 |
| Mean | 185 | | -161 | 2830 | 2350 | 17.3 | 48.45 | 6.9 | 138 | 104 | 4.3 |
| JL | 215 | | -312 | 3100 | 2630 | 17.6 | 49.39 | 6.8 | 139 | 103 | 4.6 |
| VR | 215 | | - 46 | 2290 | 1710 | 16.1 | 46.24 | 7.0 | 139 | 104 | 3.7 |
| UL | 214 | | -222 | 2990 | 2680 | 18.3 | 50.84 | 6.8 | 137 | 103 | 3.9 |
| Mean | 215 | | -193 | 2790 | 2340 | 17.3 | 48.82 | 6.9 | 138 | 103 | 4.1 |
| JL | 253 | 260 | -534 | 3040 | 2600 | 17.3 | 49.55 | 6.9 | 139 | 104 | 4.4 |
| VR | 254 | 238 | - 64 | 2340 | 1690 | 15.8 | 45.64 | 7.0 | 140 | 105 | 4.1 |
| UL | 254 | 260 | -376 | 3040 | 2670 | 18.3 | 50.47 | 6.8 | 139 | 106 | 3.8 |
| Mean | 254 | 253 | -325 | 2810 | 2320 | 17.1 | 48.55 | 6.9 | 139 | 105 | 4.1 |

Table C-II. Physical and bioclinical characteristics of subjects

| Subj. | Age | Ht. cm | Wt. kg | S.A. $m^2$ | % Body Fat | LBM kg | TBW* liters | $\dot{V}O_2$ max liters/min | HR max |
|---|---|---|---|---|---|---|---|---|---|
| RD | 43 | 179.0 | 77.05 | 1.98 | 16.1 | 64.64 | 47.3 | 2.918 | 181 |
| DE | 40 | 167.0 | 72.81 | 1.82 | 23.0 | 56.06 | 41.0 | 2.819 | 201 |
| DS | 36 | 181.6 | 78.12 | 2.00 | 7.0 | 72.65 | 53.2 | 4.272 | 181 |
| FB | 37 | 165.0 | 60.60 | 1.66 | 8.8 | 55.27 | 40.5 | 3.274 | 178 |
| BJ | 27 | 168.0 | 76.67 | 1.86 | 19.6 | 61.64 | 45.1 | 2.394 | 179 |
| DB | 21 | 185.0 | 71.05 | 1.94 | 11.3 | 63.02 | 46.1 | 2.708 | 206 |
| JL | 28 | 177.0 | 69.96 | 1.86 | 6.2 | 65.62 | 48.0 | 3.645 | 186 |
| JJ | 30 | 170.0 | 62.20 | 1.72 | 27.0 | 45.41 | 33.2 | 2.737 | 173 |
| Mean | 33 | 174.1 | 71.06 | 1.86 | 14.9 | 60.54 | 44.3 | 3.096 | 186 |
| SD | 7 | 7.5 | 6.65 | 0.12 | 7.8 | 8.22 | 6.0 | 0.609 | 12 |

*TBW = total body water estimated as 73.2% of lean body mass as suggested by Pace and Rathbun, J. Biol. Chem. 158:685-691, 1945.

Table C-III. Summary of the effects of acclimatization on work tolerance, rectal temperature, evaporative rate, and sweat electrolytes of eight men working in a hot environment (50C db, 26C wb) without fluid replacement

| | Subj. | Work Time (min) | Final $T_{RE}$ (C) | Evaporative Rate ($g/m^2$) · hr | · hr/C ↑ $T_{RE}$ > 37C | Sweat Electrolytes (mEq/liter) $Na^+$ | $Cl^-$ | $K^+$ |
|---|---|---|---|---|---|---|---|---|
| Before Acclimatization | RD | 60 | 39.70 | 454 | 168 | 85.0 | 82.0 | 6.7 |
| | DE | 92 | 39.15 | 559 | 260 | 43.0 | 35.0 | 8.4 |
| | DS | 76 | 38.67 | 748 | 448 | 86.0 | 79.0 | 6.1 |
| | FB | 108 | 39.45 | 649 | 265 | 58.0 | 53.0 | 7.4 |
| | BJ | 65 | 38.40 | 581 | 415 | 76.5 | 69.0 | 8.7 |
| | DB | 55 | 39.05 | 457 | 223 | 91.0 | 83.0 | 11.0 |
| | JL | 94 | 39.20 | 666 | 303 | 56.5 | 51.0 | 6.0 |
| | JJ | 69 | 39.20 | 568 | 258 | 67.0 | 60.0 | 8.4 |
| | Mean | 77 | 39.10 | 585 | 293 | 70.4 | 64.0 | 7.8 |
| | SD | 19 | 0.41 | 101 | 95 | 17.0 | 17.3 | 1.7 |
| After Acclimatization | RD | 90 | 38.90 | 506 | 266 | 77.0 | 73.0 | 6.3 |
| | DE | 123 | 38.89 | 604 | 320 | 28.5 | 24.0 | 6.8 |
| | DS | 70 | 38.35 | 755 | 559 | 73.0 | 60.5 | 5.8 |
| | FB | 120 | 38.78 | 645 | 362 | 34.0 | 28.0 | 5.7 |
| | BJ | 120 | 38.95 | 567 | 291 | 42.0 | 34.0 | 7.6 |
| | DB | 120 | 38.88 | 600 | 319 | 48.0 | 43.0 | 8.4 |
| | JL | 126 | 38.78 | 704 | 396 | 69.5 | 62.0 | 7.8 |
| | JJ | 125 | 38.60 | 646 | 404 | 77.5 | 70.0 | 7.8 |
| | Mean | 112 | 38.77 | 628 | 365 | 56.2 | 49.3 | 7.0 |
| | SD | 20 | 0.20 | 78 | 92 | 20.3 | 19.4 | 1.0 |

Table C-IV. Rectal temperatures of six unacclimatized men recorded at intervals during dehydrating work in the heat (50C db, 26C wb)

| Subj. | Time | $T_{RE}$ | Subj. | Time | $T_{RE}$ |
|---|---|---|---|---|---|
| RD | 2 | 37.00 | RD | 41 | 38.90 |
| DE | 2 | 37.20 | DE | 40 | 38.00 |
| FB | 2 | 37.00 | FB | 40 | 38.40 |
| BJ | 3 | 36.80 | BJ | 38 | 37.85 |
| JL | 1 | 37.20 | JL | 40 | 38.10 |
| JJ | 2 | 37.20 | JJ | 40 | 38.40 |
| Mean | 2.0 | 37.07 | Mean | 39.8 | 38.28 |
| SD | 0.6 | 0.16 | SD | 1.0 | 0.38 |
| RD | 17 | 37.90 | RD | 55 | 39.40 |
| DE | 16 | 37.50 | DE | 56 | 38.40 |
| FB | 16 | 37.40 | FB | 57 | 38.85 |
| BJ | 15 | 37.15 | BJ | 55 | 38.20 |
| JL | 15 | 37.40 | JL | 50 | 38.40 |
| JJ | 16 | 37.40 | JJ | 53 | 38.80 |
| Mean | 15.8 | 37.38 | Mean | 54.3 | 38.68 |
| SD | 0.8 | 0.12 | SD | 2.5 | 0.44 |
| RD | 21 | 38.30 | RD | 60 | 39.70 |
| DE | 31 | 37.80 | DE | 60 | 38.50 |
| FB | 30 | 37.95 | FB | 67 | 39.10 |
| BJ | 30 | 37.60 | BJ | 60 | 38.35 |
| JL | 30 | 37.80 | JL | 60 | 38.60 |
| JJ | 32 | 38.00 | JJ | 59 | 39.10 |
| Mean | 29.0 | 37.91 | Mean | 61 | 38.89 |
| SD | 4.0 | 0.24 | SD | 3 | 0.50 |

Table C-V. Rectal temperatures of six acclimatized men recorded at intervals during dehydrating work in the heat (50C db, 26C wb)

| Subj. | Time | $T_{RE}$ | Subj. | Time | $T_{RE}$ | Subj. | Time | $T_{RE}$ | Subj. | Time | $T_{RE}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| RD | 1 | 36.80 | RD | 35 | 37.60 | RD | 55 | 38.20 | RD | 85 | 38.75 |
| DE | 2 | 36.94 | DE | 36 | 37.67 | DE | 55 | 38.20 | DE | 85 | 38.55 |
| FB | 6 | 36.95 | FB | 35 | 37.88 | FB | 58 | 38.30 | FB | 88 | 38.55 |
| BJ | 2 | 37.10 | BJ | 30 | 37.63 | BJ | 60 | 38.42 | BJ | 93 | 38.58 |
| JL | 5 | 36.80 | JL | 32 | 37.40 | JL | 61 | 38.10 | JL | 96 | 38.50 |
| JJ | 5 | 37.00 | JJ | 36 | 37.50 | JJ | 65 | 37.95 | JJ | 91 | 38.25 |
| Mean | 3.5 | 36.93 | Mean | 34.0 | 37.61 | Mean | 59.0 | 38.20 | Mean | 89.7 | 38.53 |
| SD | 2.1 | 0.12 | SD | 2.5 | 0.16 | SD | 3.8 | 0.16 | SD | 4.5 | 0.16 |
| | | | | | | | | | | | |
| RD | 15 | 37.15 | RD | 41 | 37.75 | RD | 70 | 38.50 | RD | 90 | 38.90 |
| DE | 15 | 37.14 | DE | 41 | 37.75 | DE | 75 | 38.50 | DE | 100 | 38.67 |
| FB | 15 | 37.20 | FB | 43 | 38.00 | FB | 66 | 38.40 | FB | 100 | 38.62 |
| BJ | 16 | 37.38 | BJ | 44 | 37.96 | BJ | 70 | 38.50 | BJ | 104 | 38.78 |
| JL | 11 | 36.90 | JL | 40 | 37.90 | JL | 75 | 38.40 | JL | 100 | 38.50 |
| JJ | 17 | 37.10 | JJ | 44 | 37.60 | JJ | 70 | 38.00 | JJ | 100 | 38.20 |
| Mean | 14.8 | 37.15 | Mean | 42.2 | 37.83 | Mean | 71.0 | 38.38 | Mean | 99.0 | 38.61 |
| SD | 2.0 | 0.16 | SD | 1.7 | 0.16 | SD | 3.5 | 0.19 | SD | 4.7 | 0.34 |
| | | | | | | | | | | | |
| RD | 24 | 37.35 | RD | 51 | 38.00 | RD | 76 | 38.65 | | | |
| DE | 24 | 37.45 | DE | 51 | 38.00 | DE | 75 | 38.50 | | | |
| FB | 26 | 37.62 | FB | 55 | 38.25 | FB | 78 | 38.46 | | | |
| BJ | 23 | 37.50 | BJ | 49 | 38.15 | BJ | 80 | 38.54 | | | |
| JL | 25 | 37.30 | JL | 50 | 38.00 | JL | 85 | 38.40 | | | |
| JJ | 25 | 37.20 | JJ | 56 | 37.80 | JJ | 85 | 38.23 | | | |
| Mean | 24.5 | 37.40 | Mean | 52.0 | 38.03 | Mean | 79.8 | 38.46 | | | |
| SD | 1.0 | 0.15 | SD | 2.8 | 0.16 | SD | 4.4 | 0.14 | | | |

Table C-VI. Heart rates of six unacclimatized men recorded at intervals during dehydrating work in the heat (50C db, 26C wb)

| Subj. | Time | HR | Subj. | Time | HR |
|---|---|---|---|---|---|
| RD | 10 | 136 | RD | 41 | 158 |
| DE | 4 | 115 | DE | 42 | 134 |
| FB | 3 | 99 | FB | 48 | 127 |
| BJ | 6 | 115 | BJ | 39 | 142 |
| DB | 11 | 172 | DB | 38 | 200 |
| JL | 5 | 110 | JL | 40 | 127 |
| Mean | 6.5 | 124.5 | Mean | 41.3 | 148.0 |
| SD | 3.3 | 26.2 | SD | 3.6 | 28.0 |
| | | | | | |
| RD | 21 | 134 | RD | 50 | 162 |
| DE | 17 | 124 | DE | 57 | 163 |
| FB | 14 | 103 | FB | 60 | 133 |
| BJ | 14 | 134 | BJ | 57 | 134 |
| DB | 21 | 184 | DB | 51 | 194 |
| JL | 20 | 117 | JL | 50 | 133 |
| Mean | 17.8 | 132.7 | Mean | 54.2 | 153.2 |
| SD | 3.3 | 27.7 | SD | 4.4 | 24.6 |
| | | | | | |
| RD | 30 | 150 | RD | 58 | 171 |
| DE | 33 | 130 | DE | 62 | 163 |
| FB | 32 | 119 | FB | 70 | 139 |
| BJ | 21 | 141 | BJ | 57 | 134 |
| DB | 33 | 197 | DB | 55 | 191 |
| JL | 30 | 127 | JL | 60 | 137 |
| Mean | 29.8 | 144.0 | Mean | 60.3 | 155.8 |
| SD | 4.5 | 28.2 | SD | 5.3 | 22.9 |

Table C-VII. Heart rates of six acclimatized men recorded at intervals during dehydrating work in the heat (50C db, 26C wb)

| Subj. | Time | HR | Subj. | Time | HR | Subj. | Time | HR | Subj. | Time | HR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| RD | 5 | 119 | RD | 32 | 152 | RD | 52 | 156 | RD | 86 | 146 |
| DE | 2.5 | 119 | DE | 31 | 133 | DE | 66 | 146 | DE | 92 | 160 |
| FB | 5 | 98 | FB | 36 | 99 | FB | 59 | 108 | FB | 103 | 113 |
| BJ | 5 | 116 | BJ | 33 | 146 | BJ | 51 | 151 | BJ | 93 | 150 |
| DB | 6.5 | 127 | DB | 34 | 149 | DB | 58 | 161 | DB | 88 | 163 |
| JL | 5 | 102 | JL | 32 | 115 | JL | 61 | 121 | JL | 90 | 120 |
| Mean | 4.8 | 113.5 | Mean | 33.0 | 132.3 | Mean | 57.8 | 140.5 | Mean | 92.0 | 142.0 |
| SD | 1.3 | 11.1 | SD | 1.8 | 21.3 | SD | 5.6 | 21.2 | SD | 6.0 | 20.8 |
| | | | | | | | | | | | |
| RD | 13 | 131 | RD | 42 | 150 | RD | 71 | 139 | RD | 90 | 158 |
| DE | 11 | 116 | DE | 42 | 125 | DE | 70 | 152 | DE | 98 | 161 |
| FB | 16 | 104 | FB | 43 | 106 | FB | 68 | 111 | FB | 112 | 121 |
| BJ | 10 | 128 | BJ | 44 | 151 | BJ | 72 | 131 | BJ | 99 | 154 |
| DB | 15 | 146 | DB | 42 | 155 | DB | 71 | 156 | DB | 102 | 173 |
| JL | 10 | 107 | JL | 40 | 114 | JL | 75 | 118 | JL | 100 | 128 |
| Mean | 12.5 | 122.0 | Mean | 42.2 | 133.5 | Mean | 71.2 | 134.5 | Mean | 100.2 | 149.2 |
| SD | 2.6 | 16.0 | SD | 1.3 | 21.2 | SD | 2.3 | 18.0 | SD | 7.1 | 20.3 |
| | | | | | | | | | | | |
| RD | 21 | 133 | RD | 52 | 156 | RD | 76 | 141 | | | |
| DE | 23 | 133 | DE | 60 | 145 | DE | 80 | 152 | | | |
| FB | 24 | 102 | FB | 49 | 111 | FB | 88 | 119 | | | |
| BJ | 19 | 131 | BJ | 51 | 151 | BJ | 80 | 135 | | | |
| DB | 24 | 150 | DB | 53 | 161 | DB | 81 | 167 | | | |
| JL | 20 | 107 | JL | 48 | 115 | JL | 85 | 122 | | | |
| Mean | 21.8 | 126.0 | Mean | 52.2 | 139.8 | Mean | 81.7 | 139.3 | | | |
| SD | 2.1 | 18.1 | SD | 4.3 | 21.5 | SD | 4.2 | 18.2 | | | |

Table C-VIII.

| | Subj. | Work Time (min) | Weight (kg) | Weight ($\Delta$kg) | Weight ($\Delta$%) | LBM | TBW | Red Cells (ml) | Red Cells ($\Delta$ml) | Plasma (ml) | Plasma ($\Delta$ml) | Plasma ($\Delta$%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Before Acclimatization | RD | 60 | 77.051 | -0.899 | -1.17 | 64.646 | 47.32 | 2580 | -40 | 3440 | -530 | 15.4 |
| | DE | 92 | 72.812 | -1.560 | -2.14 | 56.065 | 41.04 | 2400 | -30 | 3090 | -520 | 16.8 |
| | DS | 76 | 78.121 | -1.894 | -2.42 | 72.653 | 53.18 | 3020 | -60 | 3960 | -660 | 16.7 |
| | FB | 108 | 60.599 | -1.942 | -3.20 | 55.266 | 40.45 | 2530 | -40 | 3600 | -880 | 24.4 |
| | BJ | 65 | 76.667 | -1.170 | -1.53 | 61.640 | 45.12 | 2790 | -30 | 3210 | -230 | 7.2 |
| | DB | 55 | 69.709 | -0.812 | -1.16 | 61.832 | 45.26 | 2380 | -00 | 3450 | -440 | 12.8 |
| | JL | 94 | 69.964 | -1.942 | -2.78 | 65.626 | 48.04 | 2630 | +30 | 3230 | -460 | 14.2 |
| | JJ | 69 | 62.195 | -1.124 | -1.81 | 45.402 | 33.23 | 2000 | -00 | 2850 | -450 | 15.8 |
| | Mean | 77 | 70.890 | -1.418 | -2.00 | 60.391 | 44.21 | 2541 | -21 | 3354 | -521 | 15.5 |
| | SD | 19 | 6.663 | 0.475 | 0.67 | 8.416 | 5.99 | 302 | 20 | 339 | 188 | 5.6 |
| After Acclimatization | RD | 90 | 76.525 | -1.502 | -1.96 | 64.204 | 47.00 | 2580 | -15 | 3590 | -620 | 17.3 |
| | DE | 123 | 74.712 | -2.255 | -3.02 | 57.528 | 42.11 | 2320 | -60 | 3080 | -480 | 15.6 |
| | DS | 70 | 79.385 | -1.762 | -2.22 | 73.828 | 54.04 | 2960 | -60 | 4020 | -510 | 12.7 |
| | FB | 120 | 60.490 | -2.142 | -3.54 | 55.167 | 40.38 | 2500 | -00 | 3300 | -640 | 19.4 |
| | BJ | 120 | 76.359 | -2.110 | -2.76 | 61.393 | 44.94 | 2690 | -00 | 3120 | -390 | 12.5 |
| | DB | 120 | 71.095 | -2.328 | -3.27 | 63.061 | 46.16 | 2210 | +60 | 3610 | -730 | 20.2 |
| | JL | 126 | 72.062 | -2.749 | -3.81 | 67.594 | 49.48 | 2860 | -40 | 3370 | -510 | 15.1 |
| | JJ | 125 | 62.890 | -2.314 | -3.68 | 45.910 | 33.61 | 1990 | -20 | 2790 | -550 | 19.7 |
| | Mean | 112 | 71.690 | -2.145 | -2.99 | 61.086 | 44.72 | 2514 | -17 | 3360 | -554 | 16.5 |
| | SD | 20 | 6.725 | 0.378 | 0.53 | 8.416 | 6.16 | 329 | 26 | 381 | 106 | 3.2 |

Summary of the effects of acclimatization on the changes in body weight and blood volume of eight men working in a hot environment (50C db, 26C wb) without fluid replacement

Table C-IX. Blood constituents observed in eight unacclimatized men before and at intervals during and following dehydrating work in the heat (50C db, 26C wb)

| Subj. | Sample Time (min) | Hct | Hb (g%) | Hb/Hct | Plasma Electrolytes (mEq/liter) $Na^+$ | $Cl^-$ | $K^+$ | Total (g%) | Plasma Protein Fraction Albumin | $A_1$ | $A_2$ | $\beta$ | $\gamma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CONTROL | | | | | | | | | | | | | |
| RD | 0 | 46.09 | 15.97 | .346 | 140.0 | 104.0 | 4.3 | 6.70 | 60.7 | 3.6 | 7.1 | 11.4 | 17.2 |
| DE | 0 | 46.99 | 16.75 | .356 | 142.0 | 106.0 | 3.9 | 6.20 | 57.1 | 3.3 | 7.4 | 12.4 | 12.4 |
| DS | 0 | 46.56 | 15.60 | .335 | 147.0 | 110.0 | 4.8 | 6.70 | 63.7 | 3.2 | 7.6 | 7.6 | 9.6 |
| FB | 0 | 44.35 | 16.17 | .365 | 143.0 | 106.0 | 4.0 | 6.70 | 63.1 | 2.1 | 5.6 | 7.0 | 12.5 |
| BJ | 0 | 49.98 | 17.25 | .345 | 137.0 | 104.0 | 4.4 | 7.10 | 55.8 | 2.1 | 7.1 | 11.4 | 15.0 |
| DB | 0 | 43.99 | 15.70 | .357 | 141.0 | 104.0 | 4.1 | 7.30 | 58.5 | 3.5 | 7.0 | 10.6 | 14.1 |
| JL | 0 | 48.21 | 17.05 | .354 | 135.0 | 103.0 | 8.4 | 6.65 | 56.5 | 4.1 | 7.6 | 11.8 | 12.9 |
| JJ | 0 | 44.38 | 15.10 | .340 | 140.0 | 108.0 | 4.5 | 6.60 | 59.6 | 2.2 | 7.4 | 11.0 | 13.2 |
| Mean | | 46.32 | 16.20 | .350 | 140.6 | 105.6 | 4.8 | 6.74 | 59.4 | 3.0 | 7.1 | 10.4 | 13.4 |
| SD | | 2.09 | 0.76 | .008 | 3.7 | 2.4 | 1.5 | 0.33 | 3.0 | 0.8 | 0.7 | 2.0 | 2.2 |
| WORK | | | | | | | | | | | | | |
| RD | 37 | 47.80 | 17.00 | .355 | 141.0 | 108.0 | 4.7 | 7.80 | 52.0 | 4.0 | 8.6 | 11.1 | 24.3 |
| DE | 11 | 50.14 | 17.95 | .358 | 143.0 | 108.0 | 4.4 | 6.80 | 60.2 | 2.8 | 6.4 | 12.1 | 12.1 |
| DS | 11 | 49.22 | 16.75 | .340 | 148.0 | 112.0 | 4.7 | 7.50 | 66.9 | 1.4 | 7.0 | 8.5 | 10.6 |
| FB | 14 | 48.80 | 17.25 | .353 | 143.0 | 108.0 | 4.4 | 7.10 | 60.6 | 2.7 | 6.7 | 8.7 | 12.0 |
| BJ | 11 | 51.73 | 18.00 | .348 | 140.0 | 106.0 | 4.3 | 8.00 | 54.4 | 2.7 | 7.1 | 11.5 | 14.6 |
| DB | 15 | 47.25 | 16.95 | .359 | 140.0 | 107.0 | 4.6 | 7.90 | 57.0 | 2.6 | 7.7 | 10.9 | 13.5 |
| JL | 12 | 51.05 | 17.80 | .349 | 138.0 | 104.5 | 6.6 | 7.25 | 56.6 | 3.6 | 7.7 | 11.9 | 13.1 |
| JJ | 14 | 48.26 | 16.82 | .349 | 141.0 | 109.0 | 5.4 | 7.60 | 56.9 | 3.1 | 7.7 | 10.8 | 14.6 |
| Mean | 16 | 49.29 | 17.32 | .351 | 141.8 | 107.8 | 4.9 | 7.49 | 58.1 | 2.9 | 7.4 | 10.7 | 14.4 |
| SD | 9 | 1.57 | 1.33 | .006 | 3.0 | 2.2 | 0.8 | 0.42 | 4.5 | 0.8 | 0.7 | 1.4 | 4.2 |
| RD | 60 | 50.10 | 18.27 | .359 | 142.0 | 107.0 | 4.3 | 7.90 | 58.4 | 3.9 | 7.8 | 11.7 | 18.2 |
| DE | 62 | 51.65 | 18.75 | .363 | 145.0 | 110.0 | 4.3 | 7.30 | 57.6 | 3.4 | 7.5 | 12.3 | 12.3 |
| DS | 65 | 49.55 | 16.95 | .342 | 149.0 | 111.0 | 4.3 | 7.60 | 60.3 | 2.3 | 5.8 | 8.2 | 12.3 |
| FB | 65 | 50.20 | 18.05 | .360 | 145.0 | 107.0 | 4.5 | 7.70 | 63.0 | 2.0 | 6.8 | 6.2 | 11.7 |
| BJ | 65 | 51.71 | 18.20 | .352 | 141.0 | 106.0 | 4.0 | 7.90 | 50.8 | 2.7 | 8.1 | 13.0 | 16.2 |
| DB | 46 | 47.46 | 17.42 | .367 | 140.0 | 107.0 | 4.5 | 8.05 | 60.6 | 1.4 | 6.9 | 9.7 | 13.8 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| JL | 65 | 52.39 | 18.93 | .361 | 138.0 | 106.0 | 9.0 | 7.80 | 56.2 | 3.4 | 8.0 | 11.9 | 14.2 |
| JJ | 69 | 48.83 | 16.93 | .347 | 141.0 | 108.0 | 5.1 | 7.75 | 57.7 | 3.1 | 8.1 | 10.6 | 14.3 |
| Mean | 62 | 50.24 | 17.94 | .356 | 142.6 | 107.8 | 5.0 | 7.75 | 58.1 | 2.8 | 7.4 | 10.5 | 14.1 |
| SD | 7 | 1.65 | 0.77 | .012 | 3.5 | 1.8 | 1.7 | 0.23 | 3.6 | 0.8 | 0.8 | 2.3 | 2.2 |
| RD | 60 | 50.10 | 18.27 | .359 | 142.0 | 107.0 | 4.3 | 7.90 | 58.4 | 3.9 | 7.8 | 11.7 | 18.2 |
| DE | 92 | 51.59 | 18.75 | .363 | 146.0 | 110.0 | 4.2 | 7.30 | 57.6 | 3.3 | 7.3 | 11.9 | 13.3 |
| DS | 76 | 50.86 | 17.25 | .339 | 151.0 | 115.0 | 4.4 | 8.20 | 63.9 | 2.3 | 7.0 | 8.0 | 11.3 |
| FB | 108 | 51.40 | 18.52 | .360 | 148.0 | 109.0 | 4.4 | 8.00 | 61.3 | 1.9 | 7.0 | 7.0 | 12.0 |
| BJ | 65 | 51.71 | 18.20 | .352 | 141.0 | 106.0 | 4.0 | 7.90 | 50.8 | 2.7 | 8.1 | 13.0 | 16.2 |
| DB | 55 | 47.46 | 17.42 | .367 | 140.0 | 107.0 | 4.5 | 8.05 | 60.6 | 1.4 | 6.9 | 9.7 | 13.8 |
| JL | 94 | 52.71 | 18.87 | .358 | 140.0 | 103.0 | 7.2 | 8.10 | 57.4 | 4.5 | 7.1 | 11.6 | 12.9 |
| JJ | 69 | 48.83 | 16.93 | .347 | 141.0 | 108.0 | 5.1 | 7.75 | 57.7 | 3.1 | 8.1 | 10.6 | 14.3 |
| Mean | 77 | 50.58 | 18.03 | .356 | 143.6 | 108.1 | 4.8 | 7.90 | 58.5 | 2.9 | 7.4 | 10.4 | 14.0 |
| SD | 19 | 1.72 | 0.73 | .006 | 4.2 | 3.5 | 1.0 | 0.28 | 3.8 | 3.3 | 0.5 | 2.1 | 2.3 |
| RECOVERY | | | | | | | | | | | | | |
| RD | 22 | 48.39 | 18.08 | .345 | 140.0 | 105.0 | 3.8 | 7.20 | 57.4 | 4.0 | 7.4 | 11.9 | 19.3 |
| DE | 10 | 50.91 | 18.55 | .364 | 145.0 | 109.0 | 3.9 | 7.20 | 53.2 | 4.5 | 7.8 | 12.4 | 15.0 |
| DS | 11 | 49.48 | 17.15 | .347 | 147.0 | 110.0 | 4.2 | 7.90 | 65.9 | 1.4 | 6.7 | 7.7 | 11.1 |
| FB | 14 | 49.60 | 17.85 | .360 | 149.0 | 109.0 | 3.8 | 7.65 | 59.4 | 2.7 | 7.3 | 7.3 | 14.0 |
| BJ | 11 | 50.81 | 17.75 | .349 | 141.0 | 106.0 | 3.6 | 7.60 | 54.4 | 3.5 | 7.4 | 12.9 | 14.8 |
| DB | 11 | 46.51 | 16.85 | .362 | 141.0 | 106.0 | 3.6 | 7.90 | 60.4 | 2.5 | 7.5 | 10.1 | 12.6 |
| JL | 14 | 51.07 | 18.48 | .362 | 141.0 | 105.0 | 7.9 | 7.70 | 55.2 | 4.2 | 7.9 | 12.1 | 13.9 |
| JJ | 13 | 47.29 | 16.57 | .350 | 142.0 | 107.0 | 4.2 | 7.60 | 52.7 | 3.2 | 8.5 | 12.2 | 15.4 |
| Mean | 13 | 49.26 | 17.66 | .355 | 143.3 | 107.1 | 4.4 | 7.59 | 57.3 | 3.3 | 7.6 | 10.8 | 14.5 |
| SD | 4 | 1.72 | 0.74 | .009 | 3.3 | 2.0 | 1.4 | 0.27 | 4.5 | 1.0 | 0.5 | 2.2 | 2.4 |
| RD | 22 | 48.39 | 18.08 | .345 | 143.0 | 106.0 | 4.2 | 7.00 | 51.2 | 4.2 | 7.2 | 14.5 | 22.9 |
| DE | 31 | 48.81 | 17.60 | .361 | 145.0 | 111.0 | 3.6 | 6.70 | 56.1 | 3.9 | 8.3 | 12.2 | 11.7 |
| DS | 36 | 46.75 | 16.30 | .349 | 150.0 | 114.0 | 4.3 | 7.40 | 60.4 | 3.5 | 7.5 | 8.8 | 11.9 |
| FB | 35 | 48.55 | 17.25 | .355 | 145.0 | 108.0 | 3.5 | 7.30 | 54.8 | 4.2 | 8.3 | 7.7 | 15.5 |
| BJ | 31 | 50.31 | 17.80 | .354 | 141.0 | 105.0 | 3.7 | 7.40 | 51.5 | 3.1 | 8.6 | 13.5 | 14.1 |
| DB | 33 | 45.14 | 16.25 | .360 | 141.0 | 106.0 | 3.2 | 7.70 | 56.2 | 2.4 | 7.9 | 11.0 | 15.2 |
| JL | 38 | 50.45 | 17.63 | .349 | 140.0 | 103.0 | 6.2 | 7.50 | 56.2 | 3.7 | 9.4 | 11.9 | 11.9 |
| JJ | 32 | 46.32 | 15.92 | .344 | 143.0 | 109.5 | 4.2 | 7.30 | 56.4 | 2.9 | 8.1 | 11.6 | 14.0 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mean | 32 | 48.09 | 17.10 | .352 | 143.5 | 107.8 | 4.1 | 7.29 | 55.4 | 3.5 | 8.2 | 11.4 | 14.7 |
| SD | 5 | 1.89 | 0.82 | .003 | 3.2 | 3.6 | 0.9 | 0.31 | 3.0 | 0.7 | 0.7 | 2.3 | 3.7 |
| RD | 69 | 48.76 | 17.31 | .355 | 143.0 | 106.0 | 4.2 | 7.00 | 51.2 | 4.2 | 7.2 | 14.5 | 22.9 |
| DE | 63 | 47.75 | 17.50 | .366 | 144.0 | 112.0 | 3.8 | 6.70 | 56.1 | 4.0 | 7.3 | 12.0 | 13.3 |
| DS | 61 | 48.17 | 16.55 | .344 | 147.0 | 111.0 | 4.4 | 7.40 | 64.4 | 2.3 | 5.8 | 8.2 | 12.3 |
| FB | 60 | 48.00 | 16.85 | .351 | 145.0 | 108.0 | 4.0 | 7.30 | 58.4 | 3.5 | 7.6 | 7.6 | 14.1 |
| BJ | 62 | 49.61 | 17.48 | .352 | 141.0 | 106.0 | 4.1 | 7.30 | 55.6 | 2.5 | 7.5 | 12.5 | 13.8 |
| DB | 64 | 44.27 | 15.80 | .357 | 141.0 | 107.0 | 3.5 | 7.45 | 55.5 | 3.6 | 7.8 | 11.4 | 15.1 |
| JL | 63 | 51.67 | 17.75 | .343 | 143.0 | 105.0 | 5.1 | 7.50 | 57.3 | 4.9 | 7.3 | 11.6 | 12.8 |
| JJ | 85 | 46.56 | 16.05 | .345 | 143.0 | 108.0 | 4.3 | 7.20 | 53.7 | 4.8 | 7.8 | 12.0 | 13.9 |
| Mean | 66 | 48.10 | 16.91 | .352 | 143.4 | 107.9 | 4.2 | 7.23 | 56.5 | 3.7 | 7.3 | 11.2 | 14.8 |
| SD | 8 | 2.16 | 0.72 | .011 | 2.0 | 2.5 | 0.5 | 0.27 | 3.9 | 1.0 | 0.6 | 2.3 | 3.4 |
| RD | 120 | 47.74 | 17.17 | .360 | 144.0 | 105.0 | 3.9 | 7.40 | 58.5 | 3.8 | 7.5 | 11.3 | 18.9 |
| DE | 125 | 48.36 | 17.75 | .363 | 144.0 | 110.0 | 4.0 | 6.60 | 58.2 | 3.0 | 7.3 | 12.1 | 12.1 |
| DS | 147 | 49.26 | 16.90 | .343 | 149.0 | 111.0 | 4.9 | 7.60 | 63.8 | 2.6 | 6.7 | 8.8 | 10.3 |
| FB | 120 | 48.15 | 17.35 | .360 | 145.0 | 107.0 | 4.2 | 7.30 | 55.9 | 4.0 | 7.9 | 7.3 | 15.3 |
| BJ | 122 | 50.81 | 17.65 | .347 | 142.0 | 106.0 | 4.4 | 7.70 | 54.8 | 2.1 | 7.0 | 12.5 | 14.6 |
| DB | 125 | 44.71 | 15.90 | .356 | 142.0 | 106.0 | 4.4 | 7.45 | 57.4 | 2.5 | 7.4 | 11.1 | 14.2 |
| JL | 122 | 51.40 | 17.80 | .346 | 142.0 | 103.0 | 4.5 | 7.50 | 56.0 | 4.5 | 7.6 | 11.5 | 13.4 |
| JJ | 125 | 46.82 | 16.04 | .344 | 143.0 | 107.0 | 4.4 | 7.30 | 56.9 | 3.5 | 7.6 | 11.1 | 13.2 |
| Mean | 126 | 48.41 | 17.07 | .352 | 143.9 | 106.9 | 4.3 | 7.36 | 57.7 | 3.3 | 7.4 | 10.7 | 14.0 |
| SD | 9 | 2.14 | 0.75 | .010 | 2.4 | 2.6 | 0.3 | 0.34 | 2.8 | 0.8 | 0.4 | 1.8 | 2.5 |
| RD | 190 | 47.74 | 17.17 | .360 | 144.0 | 105.0 | 3.9 | 7.40 | 58.5 | 3.8 | 7.5 | 11.3 | 18.9 |
| DE | 193 | 48.82 | 17.60 | .361 | 144.0 | 110.0 | 3.8 | 6.60 | 57.5 | 4.1 | 7.6 | 12.2 | 11.6 |
| DS | 208 | 50.85 | 16.92 | .333 | 149.0 | 111.0 | 4.9 | 7.60 | 63.8 | 2.6 | 6.7 | 8.8 | 10.3 |
| FB | 180 | 48.15 | 17.35 | .360 | 145.0 | 107.0 | 4.2 | 7.30 | 55.9 | 4.0 | 7.9 | 7.3 | 15.3 |
| BJ | 184 | 50.86 | 17.70 | .348 | 142.0 | 108.0 | 4.3 | 7.70 | 51.5 | 3.3 | 7.2 | 13.1 | 15.7 |
| DB | 185 | 44.76 | 15.80 | .353 | 142.0 | 106.0 | 4.3 | 7.40 | 58.1 | 2.7 | 8.1 | 11.5 | 12.8 |
| JL | 195 | 52.54 | 18.20 | .346 | 143.0 | 104.0 | 5.0 | 7.55 | 56.4 | 3.4 | 8.0 | 12.1 | 13.8 |
| JJ | 180 | 46.46 | 16.01 | .345 | 143.0 | 107.0 | 4.3 | 7.20 | 54.1 | 4.7 | 7.7 | 11.8 | 14.1 |
| Mean | 189 | 48.77 | 17.09 | .351 | 144.0 | 107.3 | 4.3 | 7.34 | 57.0 | 3.6 | 7.6 | 4.0 | 14.1 |
| SD | 9 | 2.56 | 0.83 | .011 | 2.3 | 2.4 | 0.4 | 0.34 | 3.6 | 0.7 | 0.5 | 1.1 | 2.7 |
| RD | 260 | 47.30 | 16.43 | .347 | 143.0 | 107.0 | 4.1 | 7.00 | 59.5 | 4.4 | 8.9 | 13.3 | 13.9 |
| DE | 273 | 48.55 | 17.65 | .364 | 144.0 | 110.0 | 4.0 | 6.70 | 56.1 | 3.6 | 7.9 | 12.2 | 13.0 |

(Table C-IX continued)

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DS | 259 | 49.83 | 16.75 | .336 | 150.0 | 112.0 | 5.0 | 7.50 | 66.9 | 3.3 | 8.3 | 6.6 | 7.7 |
| FB | 251 | 48.15 | 17.35 | .360 | 145.0 | 107.0 | 4.2 | 7.30 | 55.9 | 4.0 | 7.9 | 7.3 | 15.3 |
| BJ | 254 | 51.65 | 17.95 | .348 | 143.0 | 105.0 | 4.1 | 7.20 | 53.6 | 2.4 | 7.2 | 12.7 | 15.1 |
| DB | 243 | 45.00 | 15.98 | .355 | 142.0 | 106.0 | 4.5 | 7.65 | 57.5 | 2.5 | 7.0 | 11.4 | 14.6 |
| JL | 285 | 51.17 | 17.95 | .351 | 143.5 | 105.0 | 4.1 | 7.60 | 56.7 | 3.9 | 7.1 | 11.6 | 14.2 |
| JJ | 278 | 46.10 | 15.96 | .346 | 140.0 | 106.0 | 4.1 | 7.00 | 57.8 | 3.7 | 7.4 | 11.1 | 12.6 |
| Mean | 263 | 48.47 | 17.00 | .351 | 143.8 | 107.3 | 4.3 | 7.24 | 58.0 | 3.5 | 7.7 | 10.8 | 13.3 |
| SD | 14 | 2.34 | 0.83 | .004 | 2.9 | 2.5 | 0.3 | 0.33 | 4.0 | 0.7 | 0.7 | 2.5 | 2.5 |

(Table C-IX continued)

Table C-X. Blood constituents observed in eight acclimatized men before and at intervals during and following dehydrating work in the heat (50C db, 26C wb)

| Subj. | Sample Time (min) | Hct | Hb (g%) | Hb/Hct | Plasma Electrolytes (mEq/liter) Na$^+$ | Cl$^-$ | K$^+$ | Total (g%) | Plasma Protein Fraction Albumin | $A_1$ | $A_2$ | $\beta$ | $\gamma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CONTROL | | | | | | | | | | | | | |
| RD | 0 | 45.00 | 15.40 | .342 | 139.0 | 104.0 | 4.4 | 6.90 | 53.6 | 3.6 | 7.7 | 8.9 | 13.7 |
| DE | 0 | 45.87 | 16.50 | .360 | 144.0 | 111.0 | 4.2 | 6.40 | 60.7 | 3.5 | 6.5 | 7.7 | 21.6 |
| DS | 0 | 45.62 | 14.90 | .351 | 137.0 | 106.0 | 3.9 | 6.40 | -- | -- | -- | -- | -- |
| FB | 0 | 46.36 | 16.15 | .348 | 140.0 | 104.0 | 4.2 | 6.70 | -- | -- | -- | -- | -- |
| BJ | 0 | 49.87 | 17.10 | .341 | 141.0 | 105.0 | 4.6 | 6.90 | 54.0 | 2.4 | 7.4 | 12.3 | 15.9 |
| DB | 0 | 40.82 | 14.63 | .358 | 137.0 | 104.0 | 3.9 | -- | 59.4 | 2.9 | 7.4 | 10.9 | 12.0 |
| JL | 0 | 49.41 | 16.95 | .343 | 142.0 | 105.0 | 4.0 | 6.70 | 55.9 | 3.2 | 8.4 | 11.8 | 14.9 |
| JJ | 0 | 44.68 | 15.25 | .341 | 138.6 | 105.0 | 3.8 | 7.10 | 51.6 | 2.8 | 8.2 | 12.1 | 14.3 |
| Mean | | 45.95 | 15.86 | .348 | 139.8 | 105.5 | 4.1 | 6.73 | 55.9 | 3.1 | 7.6 | 10.6 | 15.4 |
| SD | | 2.84 | 0.94 | .005 | 2.4 | 2.3 | 0.3 | 0.26 | 3.5 | 0.5 | 0.7 | 1.9 | 3.3 |
| WORK | | | | | | | | | | | | | |
| RD | 15 | 48.35 | 16.65 | .344 | 143.0 | 109.0 | 6.1 | 7.70 | 54.5 | 3.4 | 7.3 | 8.4 | 12.9 |
| DE | 11 | 49.16 | 17.45 | .355 | 149.0 | 116.0 | 4.6 | -- | -- | -- | -- | -- | -- |
| DS | 12 | 47.74 | 16.90 | .354 | 137.0 | 106.0 | 4.3 | 7.10 | -- | -- | -- | -- | -- |
| FB | 11 | 49.73 | 17.40 | .350 | 143.0 | 106.0 | 4.5 | 7.60 | -- | -- | -- | -- | -- |
| BJ | 11 | 51.70 | 18.15 | .351 | 144.0 | 108.0 | 4.5 | 7.30 | 52.4 | 3.0 | 7.2 | 13.3 | 16.9 |
| DB | 11 | 44.86 | 16.20 | .361 | 141.0 | 108.0 | 4.2 | -- | 57.8 | 3.2 | 7.5 | 11.2 | 13.9 |
| JL | 11 | 50.71 | 17.55 | .346 | 140.0 | 107.0 | 4.3 | 7.20 | 56.2 | 3.1 | 8.6 | 12.3 | 14.2 |
| JJ | 15 | 47.32 | 16.50 | .349 | 140.5 | 106.0 | 4.3 | 7.75 | 54.0 | 3.1 | 8.1 | 11.8 | 14.9 |
| Mean | 12 | 48.70 | 17.10 | .351 | 142.2 | 108.3 | 4.6 | | | | | | |
| SD | 2 | 2.14 | 0.65 | .005 | 3.5 | 3.3 | 0.6 | | | | | | |
| RD | 60 | 49.40 | 17.05 | .345 | 144.0 | 109.0 | 6.2 | 8.20 | 56.8 | 2.4 | 6.6 | 8.4 | 11.4 |
| DE | 61 | 49.68 | 17.80 | .358 | 146.0 | 115.0 | 4.4 | 7.00 | 60.3 | 3.2 | 7.5 | 8.1 | 14.5 |
| DS | 64 | 48.61 | 16.70 | .344 | 140.0 | 106.0 | 4.1 | 7.40 | -- | -- | -- | -- | -- |
| FB | 60 | 51.11 | 17.80 | .348 | 144.0 | 105.0 | 4.4 | 7.60 | -- | -- | -- | -- | -- |
| BJ | 62 | 52.69 | 18.60 | .353 | 145.0 | 107.0 | 4.2 | 7.70 | 53.8 | 3.0 | 7.7 | 13.0 | 15.4 |
| DB | 63 | 46.56 | 17.00 | .365 | 142.0 | 109.0 | 4.3 | -- | 62.0 | 2.0 | 6.5 | 10.5 | 11.5 |
| JL | 65 | 52.21 | 18.23 | .349 | 143.0 | 108.0 | 4.3 | 7.55 | 53.3 | 4.6 | 7.9 | 11.8 | 13.8 |
| JJ | 60 | 49.19 | 17.05 | .34[illegible] | 141.6 | 106.0 | 4.2 | 8.30 | 51.8 | 3.6 | 8.1 | 12.2 | 16.7 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mean | 62 | 49.93 | 17.53 | .351 | 143.2 | 108.1 | 4.5 | 7.68 | 56.3 | 3.1 | 7.4 | 10.7 | 13.9 |
| SD | 2 | 2.01 | 0.68 | .010 | 2.0 | 3.1 | 0.7 | 0.45 | 4.1 | 0.9 | 0.7 | 2.0 | 2.1 |
| RD | 90 | 49.80 | 17.35 | .348 | 146.0 | 108.0 | 5.2 | 8.10 | 54.7 | 2.5 | 6.2 | 8.7 | 14.9 |
| DE | 123 | 50.04 | 18.30 | .366 | 152.0 | 117.0 | 4.6 | 7.60 | 61.7 | 2.4 | 7.2 | 9.0 | 11.3 |
| DS | 70 | 49.55 | 16.50 | .333 | 139.0 | 105.0 | 3.6 | 7.40 | -- | -- | -- | -- | -- |
| FB | 120 | 52.06 | 18.60 | .357 | 147.0 | 106.0 | 4.5 | 8.00 | -- | -- | -- | -- | -- |
| BJ | 120 | 53.38 | 19.25 | .361 | 146.0 | 107.0 | 4.0 | 8.10 | 51.5 | 2.5 | 7.4 | 13.5 | 15.9 |
| DB | 120 | 47.35 | 17.45 | .369 | 142.0 | 109.0 | 4.5 | -- | 58.0 | 2.8 | 7.0 | 10.7 | 14.5 |
| JL | 126 | 53.38 | 18.85 | .353 | 145.5 | 109.0 | 4.2 | 8.00 | 57.8 | 2.9 | 8.8 | 9.9 | 11.7 |
| JJ | 125 | 50.30 | 17.75 | .353 | 144.0 | 107.0 | 4.3 | 8.90 | 50.8 | 3.7 | 8.3 | 11.6 | 14.9 |
| Mean | 112 | 50.73 | 18.01 | .355 | 145.2 | 108.5 | 4.4 | 8.01 | 55.8 | 2.8 | 7.5 | 10.6 | 13.9 |
| SD | 20 | 2.08 | 0.91 | .011 | 3.8 | 3.7 | 0.5 | 0.47 | 4.2 | 0.5 | 0.9 | 1.8 | 1.9 |
| RECOVERY | | | | | | | | | | | | | |
| RD | 11 | 49.60 | 17.05 | .344 | 148.0 | 109.0 | 4.4 | 7.30 | 56.4 | 2.4 | 7.9 | 7.9 | 12.7 |
| DE | 16 | 48.70 | 17.70 | .363 | 153.0 | 117.0 | 4.5 | 7.30 | 62.2 | 2.4 | 7.2 | 8.4 | 12.6 |
| DS | 10 | 49.55 | 16.50 | .333 | 139.0 | 105.0 | 3.6 | 7.40 | -- | -- | -- | -- | -- |
| FB | 11 | 51.06 | 17.90 | .351 | 146.0 | 106.0 | 3.9 | 8.10 | -- | -- | -- | -- | -- |
| BJ | 13 | 51.96 | 18.60 | .358 | 146.0 | 109.0 | 3.8 | 7.50 | 54.1 | 3.1 | 6.7 | 12.4 | 15.0 |
| DB | 12 | 45.62 | 16.85 | .369 | 140.0 | 104.0 | 3.9 | -- | 57.1 | 3.1 | 8.2 | 11.2 | 13.8 |
| JL | 15 | 52.56 | 18.45 | .351 | 145.0 | 109.0 | 4.1 | 7.80 | 55.9 | 3.2 | 8.9 | 10.5 | 12.6 |
| JJ | 13 | 49.41 | 17.40 | .352 | 143.9 | 107.0 | 3.5 | 8.60 | 54.9 | 4.9 | 7.6 | 10.3 | 15.8 |
| Mean | 13 | 49.81 | 17.56 | .353 | 145.1 | 108.3 | 4.0 | 7.71 | 56.8 | 3.2 | 7.8 | 10.1 | 13.8 |
| SD | 2 | 2.17 | 0.75 | .013 | 4.4 | 4.0 | 0.4 | 0.49 | 2.9 | 0.9 | 0.8 | 1.7 | 1.4 |
| RD | 31 | 47.25 | 16.12 | .341 | 143.0 | 107.0 | 4.2 | 7.50 | 51.6 | 3.8 | 8.8 | 7.5 | 15.7 |
| DE | 35 | 46.91 | 17.05 | .363 | 151.0 | 117.0 | 4.3 | 6.70 | 64.6 | 3.9 | 7.9 | 6.2 | 10.1 |
| DS | 31 | 46.20 | 15.55 | .337 | 139.0 | 106.0 | 3.9 | 7.20 | -- | -- | -- | -- | -- |
| FB | 32 | 48.92 | 17.30 | .354 | 146.0 | 105.0 | 3.9 | 7.70 | -- | -- | -- | -- | -- |
| BJ | 31 | 51.37 | 18.50 | .360 | 146.0 | 109.0 | 3.8 | 7.50 | 54.1 | 3.1 | 6.7 | 12.4 | 15.0 |
| DB | 30 | 44.02 | 16.10 | .366 | 141.0 | 107.0 | 3.8 | -- | 54.5 | 3.0 | 7.7 | 12.0 | 14.2 |
| JL | 32 | 51.47 | 17.94 | .349 | 146.0 | 110.0 | 4.0 | 7.50 | 57.0 | 3.4 | 7.4 | 12.7 | 14.1 |
| JJ | 35 | 48.05 | 16.90 | .352 | 143.0 | 107.0 | 4.0 | 8.20 | 49.5 | 3.3 | 8.9 | 13.3 | 17.2 |
| Mean | 32 | 48.02 | 16.93 | .353 | 144.4 | 108.5 | 4.0 | 7.47 | 55.2 | 3.4 | 7.9 | 10.7 | 14.4 |
| SD | 2 | 2.54 | 0.99 | .009 | 3.7 | 3.8 | 0.2 | 0.46 | 5.3 | 0.4 | 0.8 | 3.0 | 2.4 |

(Table C-X continued)

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| RD | 61 | 45.70 | 15.87 | .347 | 143.0 | 108.0 | 4.2 | 7.00 | 57.6 | 2.5 | 6.3 | 8.9 | 13.3 |
| DE | 64 | 46.20 | 16.85 | .365 | 153.0 | 119.0 | 4.5 | 6.70 | 61.0 | 2.9 | 6.5 | 10.1 | 11.2 |
| DS | 65 | 46.51 | 15.70 | .338 | 142.0 | 108.0 | 4.5 | 7.30 | -- | -- | -- | -- | -- |
| FB | 63 | 48.45 | 17.00 | .351 | 146.0 | 104.0 | 3.9 | 7.70 | -- | -- | -- | -- | -- |
| BJ | 63 | 52.35 | 18.60 | .355 | 145.0 | 109.0 | 4.3 | 7.80 | 57.9 | 1.5 | 6.5 | 12.3 | 13.8 |
| DB | 61 | 43.03 | 15.60 | .363 | 143.0 | 109.0 | 4.0 | -- | 51.7 | 4.2 | 8.3 | 12.5 | 14.6 |
| JL | 63 | 51.16 | 17.77 | .347 | 145.0 | 110.0 | 3.9 | 7.30 | 55.9 | 2.5 | 8.7 | 11.8 | 14.3 |
| JJ | 64 | 47.12 | 16.45 | .349 | 140.0 | 106.0 | 4.2 | 8.00 | 53.1 | 2.8 | 8.5 | 13.0 | 14.7 |
| Mean | 63 | 47.57 | 16.73 | .352 | 144.6 | 109.1 | 4.2 | 7.40 | 56.2 | 2.7 | 7.5 | 11.4 | 13.7 |
| SD | 1 | 3.02 | 1.06 | .008 | 3.9 | 4.4 | 0.2 | 0.46 | 3.4 | 0.9 | 1.1 | 1.6 | 1.3 |
| RD | 115 | 46.05 | 15.88 | .345 | 147.0 | 110.0 | 4.1 | 7.30 | 59.2 | 2.6 | 6.0 | 8.6 | 11.8 |
| DE | 130 | 45.45 | 16.55 | .364 | 153.0 | 120.0 | 4.4 | 6.60 | 61.9 | 2.8 | 6.3 | 9.9 | 10.6 |
| DS | 123 | 47.95 | 16.10 | .336 | 141.0 | 108.0 | 4.4 | 7.00 | -- | -- | -- | -- | -- |
| FB | 127 | 49.96 | 17.50 | .350 | 146.0 | 105.0 | 4.8 | 7.80 | -- | -- | -- | -- | -- |
| BJ | 124 | 51.86 | 18.60 | .359 | 145.0 | 109.0 | 4.1 | 7.70 | 56.2 | 1.9 | 7.5 | 12.5 | 14.4 |
| DB | 121 | 44.86 | 16.20 | .361 | 144.0 | 107.0 | 4.8 | -- | 57.8 | 3.2 | 7.8 | 11.0 | 13.0 |
| JL | 133 | 50.82 | 17.57 | .346 | 144.5 | 108.0 | 4.0 | 7.40 | 56.9 | 2.5 | 8.2 | 10.8 | 14.6 |
| JJ | 115 | 47.72 | 16.60 | .348 | 141.9 | 106.0 | 4.2 | 8.00 | 56.0 | 3.0 | 7.1 | 11.3 | 15.5 |
| Mean | 124 | 48.08 | 16.88 | .351 | 145.3 | 109.1 | 4.4 | 7.40 | 58.0 | 2.7 | 7.2 | 10.7 | 13.3 |
| SD | 7 | 2.59 | 0.93 | .010 | 3.7 | 4.7 | 0.3 | 0.49 | 2.2 | 0.5 | 0.9 | 1.3 | 1.9 |
| RD | 183 | 46.35 | 15.84 | .342 | 149.0 | 108.0 | 4.1 | 7.30 | 53.2 | 2.9 | 7.4 | 9.1 | 14.3 |
| DE | 184 | 45.96 | 16.55 | .360 | 153.0 | 117.0 | 4.3 | 6.60 | 58.4 | 3.5 | 6.5 | 10.4 | 12.8 |
| DS | 189 | 47.93 | 16.30 | .340 | 141.0 | 108.0 | 4.6 | 7.60 | -- | -- | -- | -- | -- |
| FB | 190 | 49.98 | 18.05 | .361 | 145.0 | 106.0 | 5.0 | 7.90 | -- | -- | -- | -- | -- |
| BJ | 183 | 51.18 | 18.15 | .355 | 144.0 | 108.0 | 3.6 | 7.60 | 54.7 | 1.8 | 8.3 | 12.5 | 15.5 |
| DB | 187 | 45.96 | 16.25 | .354 | 143.0 | 107.0 | 4.4 | -- | 58.0 | 3.1 | 6.8 | 11.1 | 13.6 |
| JL | 188 | 51.44 | 17.94 | .349 | 144.5 | 108.0 | 4.1 | 7.40 | 56.0 | 3.8 | 8.3 | 11.5 | 14.0 |
| JJ | 183 | 48.02 | 16.45 | .343 | 143.3 | 104.0 | 4.4 | 8.00 | 54.4 | 3.5 | 8.2 | 12.9 | 14.0 |
| Mean | 186 | 48.35 | 16.94 | .351 | 145.4 | 108.3 | 4.3 | 7.49 | 55.8 | 3.1 | 7.6 | 11.3 | 14.0 |
| SD | 3 | 2.27 | 0.94 | .005 | 3.8 | 3.8 | 0.4 | 0.46 | 2.1 | 0.7 | 0.8 | 1.4 | 0.9 |
| RD | 256 | 46.90 | 15.88 | .339 | 149.0 | 107.0 | 4.2 | 7.30 | 57.2 | 2.8 | 6.2 | 8.3 | 12.4 |
| DE | 245 | 46.68 | 16.80 | .360 | 149.0 | 116.0 | 4.5 | 6.60 | 61.1 | 2.5 | 7.1 | 10.1 | 10.6 |
| DS | 270 | 48.48 | 16.40 | .338 | 140.0 | 107.0 | 3.8 | 7.40 | -- | -- | -- | -- | -- |
| FB | 255 | 49.59 | 17.85 | .360 | 145.0 | 106.0 | 4.0 | 7.80 | -- | -- | -- | -- | -- |
| BJ | 250 | 52.34 | 18.65 | .356 | 141.0 | 107.0 | 3.9 | 7.80 | 52.6 | 3.5 | 8.7 | 12.7 | 15.0 |

(Table C-X continued)

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DB | 255 | 45.25 | 16.40 | .362 | 144.0 | 108.0 | 4.8 | -- | 58.5 | 2.6 | 7.8 | 11.0 | 12.3 |
| JL | 275 | 51.13 | 17.80 | .348 | 145.5 | 108.0 | 3.8 | 7.40 | 58.1 | 3.4 | 8.1 | 11.5 | 11.5 |
| JJ | 253 | 48.26 | 16.75 | .347 | 142.0 | 105.0 | 4.2 | 8.30 | 56.3 | 2.6 | 7.3 | 10.6 | 14.6 |
| Mean | 257 | 48.58 | 17.07 | .351 | 144.4 | 108.0 | 4.2 | 7.51 | 57.3 | 2.9 | 7.5 | 10.7 | 12.7 |
| SD | 10 | 2.37 | 0.94 | .012 | 3.4 | 3.4 | 0.4 | 0.53 | 2.8 | 0.4 | 0.9 | 1.5 | 1.7 |

(Table C-X continued)

Table C-XI. Estimated plasma volume changes in eight unacclimatized men at intervals during and following dehydrating work in the heat (50C db, 26C wb)

| Subj. | Sample Time (min) | Red Blood Cells ml | Red Blood Cells Δml | Plasma ml | Plasma Δml |
|---|---|---|---|---|---|
| CONTROL | | | | | |
| RD | 0 | 2580 | | 3440 | |
| DE | 0 | 2400 | | 3090 | |
| DS | 0 | 3020 | | 3960 | |
| FB | 0 | 2530 | | 3600 | |
| BJ | 0 | 2790 | | 3210 | |
| DB | 0 | 2380 | | 3450 | |
| JL | 0 | 2630 | | 3230 | |
| JJ | 0 | 2000 | | 2850 | |
| Mean | | 2541 | | 3354 | |
| SD | | 302 | | 339 | |
| WORK | | | | | |
| RD | 37 | | | 3190 | -250 |
| DE | 11 | | | 2740 | -350 |
| DS | 11 | | | 3550 | -410 |
| FB | 14 | | | 3030 | -570 |
| BJ | 11 | | | 2980 | -230 |
| DB | 15 | | | 3040 | -410 |
| JL | 12 | | | 2920 | -310 |
| JJ | 14 | | | 2460 | -390 |
| Mean | 16 | | | 2989 | -365 |
| SD | 9 | | | 318 | 108 |
| RD | 60 | | | 2910 | -530 |
| DE | 60 | | | 2580 | -510 |
| DS | 65 | | | 3490 | -470 |
| FB | 65 | | | 2850 | -750 |
| BJ | 65 | | | 2980 | -230 |
| DB | 46 | | | 3010 | -440 |
| JL | 65 | | | 2790 | -440 |
| JJ | 69 | | | 2400 | -450 |
| Mean | 62 | | | 2876 | -478 |
| SD | 7 | | | 323 | 143 |
| RD | 60 | | | 2910 | -530 |
| DE | 92 | | | 2570 | -520 |
| DS | 76 | | | 3300 | -660 |
| FB | 108 | | | 2720 | -880 |
| BJ | 65 | | | 2980 | -230 |
| DB | 55 | | | 3010 | -440 |
| JL | 94 | | | 2770 | -460 |
| JJ | 69 | | | 2400 | -450 |

| | | | |
|---|---|---|---|
| Mean | 77 | 2833 | -521 |
| SD | 19 | 280 | 188 |
| RECOVERY | | | |
| RD | 22 | 3080 | -360 |
| DE | 10 | 2620 | -470 |
| DS | 11 | 3450 | -510 |
| FB | 14 | 2890 | -710 |
| BJ | 11 | 3060 | -150 |
| DB | 11 | 3120 | -330 |
| JL | 14 | 2950 | -280 |
| JJ | 13 | 2550 | -300 |
| Mean | 13 | 2965 | -389 |
| SD | 4 | 288 | 171 |
| RD | 22 | 3080 | -360 |
| DE | 31 | 2820 | -270 |
| DS | 36 | 3800 | -160 |
| FB | 35 | 2990 | -610 |
| BJ | 31 | 3100 | -110 |
| DB | 33 | 3290 | -160 |
| JL | 38 | 3030 | -200 |
| JJ | 32 | 2640 | -210 |
| Mean | 32 | 3094 | -260 |
| SD | 5 | 345 | 161 |
| RD | 69 | 3025 | -415 |
| DE | 63 | 2930 | -160 |
| DS | 61 | 3570 | -390 |
| FB | 60 | 3030 | -570 |
| BJ | 62 | 3170 | - 40 |
| DB | 64 | 3400 | - 50 |
| JL | 63 | 2910 | -320 |
| JJ | 85 | 2620 | -230 |
| Mean | 66 | 3082 | -272 |
| SD | 8 | 297 | 186 |
| RD | 120 | 3130 | -310 |
| DE | 125 | 2850 | -240 |
| DS | 147 | 3410 | -550 |
| FB | 120 | 3010 | -590 |
| BJ | 122 | 3010 | -200 |
| DB | 125 | 3340 | -110 |
| JL | 122 | 2950 | -280 |
| JJ | 125 | 2590 | -260 |
| Mean | 126 | 3036 | -318 |
| SD | 9 | 263 | 167 |

(Table C-XI continued)

| | | | | | |
|---|---|---|---|---|---|
| RD | 190 | | | 3130 | -310 |
| DE | 193 | | | 2790 | -300 |
| DS | 208 | | | 3190 | -770 |
| FB | 180 | | | 3010 | -590 |
| BJ | 184 | | | 2990 | -220 |
| DB | 185 | | | 3340 | -110 |
| JL | 195 | | | 2840 | -390 |
| JJ | 180 | | | 2630 | -220 |
| Mean | 189 | | | 2990 | -364 |
| SD | 9 | | | 231 | 217 |
| | | | | | |
| RD | 260 | 2480 | -100 | 3130 | -310 |
| DE | 273 | 2300 | -100 | 2800 | -290 |
| DS | 259 | 2830 | -190 | 3270 | -690 |
| FB | 251 | 2430 | -100 | 3000 | -600 |
| BJ | 254 | 2670 | -120 | 2890 | -320 |
| DB | 243 | 2370 | - 10 | 3340 | -110 |
| JL | 285 | 2720 | + 90 | 3000 | -230 |
| JJ | 278 | 2020 | + 20 | 2690 | -160 |
| Mean | 263 | 2478 | - 64 | 3015 | -339 |
| SD | 14 | 260 | 90 | 224 | 204 |

(Table C-XI continued)

Table C-XII. Estimated plasma volume changes in eight acclimatized men at intervals during and following dehydrating work in the heat (50C db, 26C wb)

| Subj. | Sample Time (min) | Red Blood Cells ml | Red Blood Cells $\Delta$ml | Plasma ml | Plasma $\Delta$ml |
|---|---|---|---|---|---|
| CONTROL | | | | | |
| RD | 0 | 2580 | | 3590 | |
| DE | 0 | 2320 | | 3080 | |
| DS | 0 | 2960 | | 4020 | |
| FB | 0 | 2500 | | 3300 | |
| BJ | 0 | 2690 | | 3120 | |
| DB | 0 | 2210 | | 3610 | |
| JL | 0 | 2860 | | 3370 | |
| JJ | 0 | 1990 | | 2790 | |
| Mean | | 2514 | | 3360 | |
| SD | | 329 | | 381 | |
| WORK | | | | | |
| RD | 15 | | | 3150 | -440 |
| DE | 11 | | | 2730 | -350 |
| DS | 12 | | | 3670 | -350 |
| FB | 11 | | | 2910 | -390 |
| BJ | 11 | | | 2900 | -220 |
| DB | 11 | | | 3120 | -490 |
| JL | 11 | | | 3190 | -180 |
| JJ | 15 | | | 2530 | -260 |
| Mean | 12 | | | 3025 | -335 |
| SD | 2 | | | 344 | 108 |
| RD | 60 | | | 3020 | -570 |
| DE | 61 | | | 2660 | -420 |
| DS | 64 | | | 3510 | -510 |
| FB | 60 | | | 2760 | -540 |
| BJ | 62 | | | 2800 | -320 |
| DB | 63 | | | 2950 | -660 |
| JL | 65 | | | 3000 | -370 |
| JJ | 60 | | | 2340 | -450 |
| Mean | 62 | | | 2880 | -480 |
| SD | 2 | | | 337 | 112 |
| RD | 90 | | | 2970 | -620 |
| DE | 123 | | | 2600 | -480 |
| DS | 70 | | | 3360 | -660 |
| FB | 120 | | | 2660 | -340 |
| BJ | 120 | | | 2730 | -390 |
| DB | 120 | | | 2880 | -730 |
| JL | 126 | | | 2860 | -510 |
| JJ | 125 | | | 2240 | -540 |
| Mean | 112 | | | 2788 | -534 |
| SD | 20 | | | 323 | 133 |

RECOVERY

| | | | |
|---|---|---|---|
| RD | 11 | 2990 | -600 |
| DE | 16 | 2710 | -370 |
| DS | 10 | 3360 | -660 |
| FB | 11 | 2760 | -240 |
| BJ | 13 | 2880 | -240 |
| DB | 12 | 3110 | -500 |
| JL | 15 | 2940 | -430 |
| JJ | 13 | 2310 | -480 |
| Mean | 13 | 2883 | -440 |
| SD | 2 | 309 | 153 |
| RD | 31 | 3260 | -330 |
| DE | 35 | 2870 | -210 |
| DS | 31 | 3780 | -240 |
| FB | 32 | 2990 | -310 |
| BJ | 31 | 2940 | -180 |
| DB | 30 | 3330 | -280 |
| JL | 32 | 3040 | -330 |
| JJ | 35 | 2420 | -370 |
| Mean | 32 | 3079 | -281 |
| SD | 2 | 395 | 66 |
| RD | 61 | 3450 | -140 |
| DE | 64 | 2920 | -160 |
| DS | 65 | 3710 | -310 |
| FB | 63 | 3050 | -250 |
| BJ | 63 | 2830 | -290 |
| DB | 61 | 3490 | -120 |
| JL | 63 | 3060 | -310 |
| JJ | 64 | 2500 | -290 |
| Mean | 63 | 3126 | -234 |
| SD | 1 | 398 | 81 |
| RD | 115 | 3400 | -190 |
| DE | 130 | 2980 | -100 |
| DS | 123 | 3480 | -540 |
| FB | 127 | 2880 | -420 |
| BJ | 124 | 2890 | -230 |
| DB | 121 | 3280 | -330 |
| JL | 133 | 3090 | -280 |
| JJ | 115 | 2430 | -360 |
| Mean | 124 | 3054 | -306 |
| SD | 7 | 339 | 138 |
| RD | 183 | 3350 | -240 |
| DE | 184 | 2890 | -190 |
| DS | 189 | 3440 | -580 |
| FB | 190 | 2880 | -420 |
| BJ | 183 | 2960 | -160 |

(Table C-XII continued)

| | | | | | |
|---|---|---|---|---|---|
| DB | 187 | | | 3190 | -420 |
| JL | 188 | | | 3000 | -370 |
| JJ | 183 | | | 2390 | -400 |
| Mean | 186 | | | 3013 | -348 |
| SD | 3 | | | 328 | 141 |
| | | | | | |
| RD | 256 | 2530 | - 50 | 3260 | -330 |
| DE | 245 | 2130 | -190 | 2780 | -300 |
| DS | 270 | 2730 | -230 | 3330 | -690 |
| FB | 255 | 2520 | + 20 | 2940 | -360 |
| BJ | 250 | 2680 | - 10 | 2820 | -300 |
| DB | 255 | 2410 | -210 | 3320 | -290 |
| JL | 275 | 2740 | -120 | 3030 | -340 |
| JJ | 253 | 1920 | - 70 | 2360 | -430 |
| Mean | 258 | 2458 | -106 | 2980 | -380 |
| SD | 10 | 295 | 93 | 332 | 133 |

(Table C-XII continued).

Table C-XIII. UNACCLIMATIZED

| Subj. | Urine Flow Total ml | ml/min | Urine Electrolytes $Na^+$ | mEq/hr | $Cl^-$ | mEq/hr | $K^+$ | mEq/hr | Urine Specific Gravity | pH | Osmolality mOsmal/liter |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Control** | | | | | | | | | | | |
| RD | 1375 | 1.53 | 70.0 | 6.43 | 55.0 | 5.05 | 16.7 | 1.53 | 1.009 | 5.0 | 411.2 |
| DE | 1150 | 1.18 | 28.5 | 2.02 | 27.0 | 1.91 | 44.0 | 3.12 | 1.012 | 8.0 | 447.1 |
| DS | 690 | 0.87 | 115.5 | 6.03 | 77.0 | 4.02 | 31.0 | 1.62 | 1.020 | 6.0 | 831.3 |
| FB | 340 | 0.49 | 206.0 | 6.06 | 195.0 | 5.73 | 88.0 | 2.59 | 1.021 | 6.5 | 937.0 |
| BJ | 530 | 0.59 | 147.0 | 5.20 | 128.0 | 4.53 | 30.0 | 1.06 | 1.020 | 5.0 | -- |
| DB | 418 | 0.47 | 146.0 | 4.12 | 123.0 | 3.47 | 58.0 | 1.64 | 1.024 | 6.0 | 940.6 |
| JL | 720 | 0.88 | 74.0 | 3.91 | 79.0 | 4.17 | 22.0 | 1.16 | 1.011 | 5.0 | 438.0 |
| JJ | 710 | 0.66 | 213.0 | 8.43 | 189.0 | 7.48 | 102.0 | 4.04 | 1.024 | 5.0 | 982.1 |
| Mean | | 0.83 | | 5.28 | | 4.55 | | 2.10 | 1.018 | 5.8 | 712.5 |
| SD | | 0.37 | | 1.94 | | 1.64 | | 1.05 | 0.006 | 1.1 | 352.5 |
| **Dehydrating Work** | | | | | | | | | | | |
| RD | 118 | 0.34 | 118.0 | 2.41 | 128.0 | 2.61 | 111.0 | 2.26 | 1.022 | 5.0 | 784.0 |
| DE | 130 | 0.34 | 78.5 | 1.60 | 70.0 | 1.43 | 133.0 | 2.71 | 1.022 | 6.0 | 771.0 |
| DS | 125 | 0.31 | 124.5 | 2.32 | 158.0 | 2.94 | 133.0 | 2.47 | 1.029 | 6.0 | 1049.3 |
| FB | 86 | 0.23 | 136.0 | 1.88 | 188.0 | 2.59 | 189.0 | 2.61 | 1.019 | 6.0 | 1015.1 |
| BJ | 120 | 0.36 | 127.0 | 2.74 | 290.0 | 6.26 | 144.0 | 3.11 | 1.024 | 5.0 | -- |
| DB | 82 | 0.25 | 117.0 | 1.76 | 139.0 | 2.09 | 129.0 | 1.94 | 1.030 | 6.0 | 1059.7 |
| JL | 95 | 0.24 | 109.0 | 1.57 | 140.0 | 2.02 | 103.0 | 1.48 | 1.024 | 5.0 | 836.0 |
| JJ | 127 | 0.35 | 265.0 | 5.57 | 246.0 | 5.17 | 74.0 | 1.55 | 1.026 | 5.0 | 1136.6 |
| Mean | | 0.30 | | 2.48 | | 3.14 | | 2.27 | 1.025 | 5.5 | 950.2 |
| SD | | 0.05 | | 1.32 | | 1.68 | | 0.57 | 0.004 | 0.5 | 363.2 |

Urine parameters observed in eight unacclimatized men in the post-absorptive control state and again following a bout of dehydrating work in the heat (50C db, 26C wb)

Table C-XIV. ACCLIMATIZED

| Subj. | Urine Flow Total ml | ml/min | Urine Electrolytes $Na^+$ | mEq/hr | $Cl^-$ | mEq/hr | $K^+$ | mEq/hr | Specific Gravity | Urine pH | Osmolality mOsmal/liter |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Control** | | | | | | | | | | | |
| RD | 1600 | 1.67 | 74.5 | 7.46 | 70.0 | 7.01 | 24.0 | 2.40 | 1.017 | 5.0 | 298.7 |
| DE | 610 | 0.67 | 87.0 | 3.50 | 79.0 | 3.18 | 76.0 | 3.06 | 1.020 | 6.0 | 795.3 |
| DS | 800 | 1.05 | 130.0 | 8.19 | 107.0 | 6.74 | 42.0 | 2.65 | 1.023 | 6.0 | 966.6 |
| FB | 480 | 0.55 | 186.0 | 6.14 | 148.0 | 4.88 | 62.0 | 2.05 | 1.023 | 6.0 | 917.1 |
| BJ | 155 | 0.97 | 168.0 | 9.78 | 220.0 | 12.80 | 100.0 | 5.82 | 1.027 | 5.0 | 1133.1 |
| DB | 320 | 0.51 | 154.0 | 4.71 | 132.0 | 4.04 | 63.0 | 1.93 | 1.027 | 6.0 | 1091.5 |
| JL | 492 | 0.60 | 172.0 | 6.19 | 136.0 | 4.90 | 33.0 | 1.19 | 1.026 | 6.0 | 983.4 |
| JJ | 1050 | 1.18 | 207.0 | 14.66 | 179.0 | 12.67 | 28.0 | 1.98 | 1.012 | 5.0 | 567.4 |
| Mean | | 0.90 | | 7.58 | | 7.03 | | 2.64 | 1.022 | 5.6 | 844.1 |
| SD | | 0.40 | | 3.47 | | 3.74 | | 1.40 | 0.005 | 0.5 | 283.1 |
| **Dehydrating Work** | | | | | | | | | | | |
| RD | 146 | 0.34 | 159.0 | 3.24 | 127.0 | 2.59 | 145.0 | 2.96 | 1.021 | 7.0 | 764.3 |
| DE | 165 | 0.41 | 162.0 | 3.99 | 175.0 | 4.31 | 107.0 | 2.63 | 1.021 | 7.0 | 1012.0 |
| DS | 170 | 0.46 | 140.0 | 3.86 | 179.0 | 4.94 | 122.0 | 3.37 | 1.027 | 6.0 | 1135.4 |
| FB | 115 | 0.29 | 124.0 | 2.16 | 200.0 | 3.48 | 210.0 | 3.65 | 1.028 | 6.0 | 1077.7 |
| BJ | 27 | 0.23 | 59.5 | 0.82 | 198.0 | 2.73 | 194.0 | 2.68 | 1.030 | 5.0 | 1083.0 |
| DB | 95 | 0.35 | 148.0 | 3.11 | 146.0 | 3.07 | 99.0 | 2.08 | 1.031 | 6.0 | 1213.0 |
| JL | 132 | 0.33 | 165.0 | 3.27 | 214.0 | 4.24 | 95.0 | 1.88 | 1.029 | 6.0 | 1049.7 |
| JJ | 86 | 0.33 | 106.0 | 2.10 | 107.0 | 2.12 | 121.0 | 2.40 | 1.021 | 5.0 | 752.4 |
| Mean | | 0.34 | | 2.82 | | 3.44 | | 2.71 | 1.026 | 6.0 | 1010.9 |
| SD | | 0.07 | | 1.06 | | 0.98 | | 0.61 | 0.004 | 0.8 | 167.0 |

Urine parameters observed in eight acclimatized men in the post-absorptive control state and again following a bout of dehydrating work in the heat (50C db, 26C wb)

Table C-XV

| Subject | Hb g% | Hct | Hb/Hct | COHb % saturation |
|---|---|---|---|---|
| JL 1 | 17.1 | 48.2 | 0.354 | 0.828 |
| 2 | 17.0 | 49.4 | 0.343 | 0.924 |
| 3 | 17.2 | 48.3 | 0.356 | 1.129 |
| RD 1 | 16.1 | 46.1 | 0.349 | 0.855 |
| 2 | 15.4 | 45.0 | 0.342 | 0.879 |
| JJ 1 | 15.1 | 44.4 | 0.340 | 0.944 |
| 2 | 15.3 | 44.7 | 0.341 | 0.829 |
| FB 1 | 16.3 | 44.4 | 0.368 | 1.005 |
| 2 | 16.2 | 46.4 | 0.348 | 1.243 |
| DB 1 | 15.7 | 44.0 | 0.357 | 1.091 |
| 2 | 14.6 | 40.8 | 0.358 | 1.131 |
| BJ 1 | 17.3 | 49.9 | 0.346 | 0.938 |
| 2 | 17.1 | 49.9 | 0.343 | 1.233 |
| RE 1 | 16.8 | 47.0 | 0.356 | 1.067 |
| 2 | 16.5 | 45.9 | 0.360 | 0.918 |
| DS 1 | 15.6 | 46.6 | 0.335 | 0.919 |
| 2 | 14.9 | 45.6 | 0.327 | 0.864 |
| VR 1 | 16.3 | 47.1 | 0.346 | 1.100 |
| Mean | 16.1 | 46.3 | 0.348 | 0.994 |
| SD | 0.8 | 2.3 | 0.010 | 0.135 |

Blood observations on 9 healthy men residing in Albuquerque (B = 630 mm Hg). Samples were drawn after 60 minutes rest in the post-absorptive state. Repeated determinations on the same subjects were made after 10 days or more.

Table C-XVI. Time course of CO elimination for three healthy men breathing room air while resting in a hot environment (50C db, 25C wb) with fluid replacement.

| Subject | Elapsed Time (min) | %COHb $C_0$ | %COHb $C_M$ | %COHb $C_t$ | $\frac{C_t - C_0}{C_M - C_0}$ |
|---|---|---|---|---|---|
| JL | 30 | 1.155 | 5.681 | 5.080 | 0.866 |
| | 71 | 1.155 | 5.681 | 4.819 | 0.809 |
| | 131 | 1.155 | 5.681 | 4.509 | 0.740 |
| | 191 | 1.155 | 5.681 | 4.055 | 0.640 |
| | 221 | 1.155 | 5.681 | 3.942 | 0.615 |
| VR | 8 | 1.106 | 7.996 | 7.549 | 0.935 |
| | 24 | 1.106 | 7.996 | 7.130 | 0.874 |
| | 38 | 1.106 | 7.996 | 7.043 | 0.862 |
| | 68 | 1.106 | 7.996 | 6.682 | 0.809 |
| | 127 | 1.106 | 7.996 | 6.340 | 0.760 |
| | 188 | 1.106 | 7.996 | 5.559 | 0.646 |
| | 218 | 1.106 | 7.996 | 5.289 | 0.607 |
| | 243 | 1.106 | 7.996 | 5.205 | 0.595 |
| UL | 8 | 1.131* | 7.407 | 7.223 | 0.971 |
| | 25 | 1.131 | 7.407 | 6.543 | 0.862 |
| | 39 | 1.131 | 7.407 | 6.316 | 0.826 |
| | 63 | 1.131 | 7.407 | 6.234 | 0.813 |
| | 130 | 1.131 | 7.407 | 5.528 | 0.701 |
| | 189 | 1.131 | 7.407 | 5.140 | 0.639 |
| | 216 | 1.131 | 7.407 | 4.940 | 0.607 |
| | 244 | 1.131 | 7.407 | 4.866 | 0.595 |

*UL is a pipe smoker. $C_0$ was estimated by averaging the non-smokers' $C_0$ in this study.

$C_0$ = % COHb while at rest and post-absorptive before rebreathing with CO

$C_M$ = % COHb of men following 10 minutes of rebreathing a measured quantity of CO added to a rebreathing apparatus

$C_t$ = % COHb at specified time after subject was taken off the rebreathing apparatus

## D. RE-EVALUATION OF THE OPEN-CIRCUIT METHOD FOR MEASURING METABOLIC RATE WITH REGARD TO THE ALLEGED METABOLIC PRODUCTION OF GASEOUS NITROGEN

Indirect calorimetry by the open circuit method as introduced by Zuntz, et. al., (8) and later much improved by Douglas (5) and Haldane (6) has continued to be the method of choice for studies of metabolic rate in the laboratory, in the field, and at the bedside for the past 60 years. Particularly the ingenious expedient proposed by Haldane to use the ratio between expired and inspired nitrogen fraction, which is a function of the respiratory exchange ratio, to estimate the inspired ventilation as:

$$\dot{V}_I = \dot{V}_E \times F_{EN_2} / F_{IN_2} \tag{1}$$

reduced the measurements necessary for the calculation to the expired ventilation and the analysis of expired gas for oxygen and carbon dioxide. This transformation is based on the assumption that the amount of nitrogen exhaled is equal to that inhaled in any reasonably steady state.

Of late, reports have been published that challenge the latter premise in that nitrogen indeed contributes to gas exchange from unknown metabolic sources, especially during exercise (1,2,3,7), thereby casting doubt on the validity of Haldane's calculation of metabolic rate.

The present tests were undertaken to ascertain whether or not the results of metabolic rate measurements, as routinely employed in this laboratory, were significantly different when using a direct measurement of the inspired ventilation rather than estimated by the Haldane transformation (Eq. 1).

### Procedure

Six subjects performed a total of 53 tests on a von Döbeln (4) bicycle ergometer. They were on their usual diet and tests were performed one or more times a day, some before, others after meals. Some had exercised vigorously some time before the tests, others had not. Three subjects were accustomed to exercise regularly, the other three were not. A work load was chosen for each subject corresponding to 40-50% of his aerobic capacity, but primarily at a level at which he could maintain an approximately sine-wave breathing pattern in cadence with the pedalling rhythm which was

given by metronome (50 rpm). This was very important in order to match inspiratory and expiratory tidal volumes while switching into and out of the two Tissot spirometers. The latter was accomplished unobserved by the subject. A low deadspace respiratory valve (Hans Rudolph # 1700) was used throughout. Although this valve has a relatively high resistance for exercise, it was the only one of several tested that had absolutely no backlash. Both spirometers were calibrated by transferring 50 liters of air with a calibrated 1 liter (Hamilton) syringe through the Rudolph valve from one spirometer to the other repeatedly. The spirometer factors were 173.3 ml/mm for the inspiratory and 133.3 ml/mm for the expiratory Tissot. The inspiratory Tissot was filled by bubbling air under pressure through a fine metal screen under water in a large carboy to insure saturation with water vapor. The small thermometers supplied with the spirometers were replaced by mercury thermometers graduated to 0.2 C. The temperature readings were found to be extremely critical for the conversion to STPD. Thermal effects from air conditioning outlets and light fixtures in the immediate vicinity of the spirometers were minimized. Preliminary tests revealed consistent temperature transients over many minutes after filling the spirometers either from the air source or with expired gas. Therefore, volume, temperature and barometric readings were taken not less than 15 minutes after filling and after each test to insure adequate temperature and water vapor stabilization. Reductions from ATPS conditions to STPD were calculated assuming complete saturation with water vapor at measured temperatures. The subjects worked for 5 minutes at their chosen work load with mouthpiece in place, whereupon inspired and expired ventilation was measured over another two minutes. During the latter, expired air was sampled slowly and continuously from the stopcock on the inlet pipe of the expiratory spirometer with a 1 liter (Hamilton) gas-tight syringe. Gas analyses were performed with a Medical Mass-Spectrometer (MMS-8, Scientific Research Instruments Corp.) which was calibrated for each sample with gas analyzed by the Scholander method.

The results from all 53 tests were pooled and the data for inspired ventilation as calculated with Eq. 1 and measured directly as well as for

the oxygen consumption derived from either the former or the latter were analyzed by paired comparison. The Student's t-test for significance was applied separately to the differences in each set of pairs.

## Results and Conclusions

Table I summarizes the statistics on the comparison between the two methods for determining inspiratory ventilation, A the Haldane method, B the direct measurement, and the difference A-B. Table II presents a similar arrangement for the oxygen consumption. The difference A-B for inspired ventilation was less than 0.5% in 51 out of 53 pairs and more than 1% in only one instance. The difference in oxygen consumption was less than 1% of the value measured in 38 instances and greater than 2% in only two cases. In view of the essentially random distribution of the differences, as shown at the bottom of both tables, and the high P-values obtained for the mean differences in both comparisons, there is no valid reason to reject the hypothesis that the differences observed in the results are attributable entirely to random errors in measurement and that no true difference exists.

Obviously some inequality in the amount of nitrogen inspired and expired, either one way or the other, can be calculated for all of the 53 tests, because in no instance was the inspired ventilation measured directly exactly equal to the Haldane value. A tabulation of such data has been omitted because it would be redundant. Suffice it to say that the difference between inspired and expired nitrogen calculated from the mean values for $\dot{V}_I$ direct (Table I), the mean expired ventilation (27030 ml/min) and the mean expired nitrogen fraction (.7926) amounts to -2 ml/min. The same considerations regarding the significance of this difference apply here as to the difference in mean oxygen consumption.

While the possibility of gaseous nitrogen uptake or elimination by the lungs cannot be ruled out by these experiments, its effects on metabolic rate measurements is apparently well within the errors of measurement of the procedures employed. This is reassuring because the determination of respiratory gas exchange using the Haldane transformation is much less complicated. Furthermore, it stands to reason that the use of a second

volumetric device for the inspired ventilation inevitably adds to the errors of measurement.


Summary

Paired comparisons were made in 53 tests between $\dot{V}_{O2}$ derived by the Haldane transformation and by direct measurement of $\dot{V}_I$. Six subjects worked on a bicycle ergometer at work loads requiring between 1100 and 2300 ml/min $\dot{V}_{O2}$ for 5 min. Then $\dot{V}_I$ and $\dot{V}_E$ were measured with two 120 liter Tissot spirometers for 2 min while aliquot samples of expired gas were collected for analysis. Subjects were on their usual diet and worked before or after meals. Spirometer temperatures were read within 0.1 C after 15 min equilibration and gas volumes reduced to STPD assuming 100% RH. Mean $\dot{V}_{O2}$ estimated according to Haldane was 1581 ml/min and 1580 using $\dot{V}_I$ measured directly with a mean difference and SE of 1 ± 2.5 ml/min. In 3 tests out of 53 results were equal, in 27 the direct measurements were higher and in 23 lower than the indirect estimate. It is concluded that if $N_2$ inequality exists, it is not of sufficient magnitude to vitiate the estimate of $\dot{V}_{O2}$ measuring expired ventilation only.

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5. Douglas, C.G. A method for determining the total respiratory gas exchange in man. J. Physiol. (Lond.) 42: xvii, 1911.

6. Haldane, J.S. Methods of air analysis. Griffin & Co., London, 1912.

7. Muysers, K. Gibt es eine Stickstoffabgabe in der menschlichen Lunge? Pflügers Arch. 317:157-172, 1970.

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Table D-I

INSPIRATORY VENTILATION (ml/min STPD)*

| | A. Haldane | B. Direct | A - B |
|---|---|---|---|
| Range | 17208 - 36662 | 17184 - 36582 | +274 to -341 |
| Mean | 27112 | 27106 | +6 |
| SD | 4831 | 4827 | 86 |
| S.E.M. | 664 | 663 | 12 |
| t-test | -- | -- | P = 0.58 |

n = 53 with 28 A > B and 25 A < B

Table D-II

OXYGEN CONSUMPTION (ml/min STPD)*

| | A. Haldane | B. Direct | A - B |
|---|---|---|---|
| Range | 1108 - 2329 | 1097 - 2312 | +57 to -72 |
| Mean | 1581 | 1580 | +1 |
| SD | 373 | 375 | 18 |
| S.E.M. | 51 | 52 | 2.5 |
| t-test | -- | -- | P = 0.68 |

n = 53 with 23 A > B, 3 A = B, and 27 A < B

SD: standard deviation; S.E.M.: standard error of mean

Table D-III

PAIRED COMPARISON OF INSPIRED VOLUME CALCULATED WITH THE HALDANE TRANSFORMATION AND MEASURED DIRECTLY.

| | | ml/min (STPD) | | |
|---|---|---|---|---|
| Subj. | Test No. | Hald. | dir. | diff. |
| I | 1. | 31703 | 31621 | +82 |
| | 2. | 26520 | 26420 | +100 |
| | 3. | 27402 | 27382 | +20 |
| | 4. | 27076 | 27078 | -2 |
| | 5. | 28325 | 28371 | -46 |
| | 6. | 28119 | 28073 | +46 |
| | 7. | 27780 | 27913 | -133 |
| | 8. | 30093 | 29976 | +117 |
| | 9. | 29156 | 29189 | -33 |
| | 10. | 29418 | 29281 | +137 |
| II | 11. | 23677 | 23711 | -34 |
| | 12. | 24993 | 25027 | -34 |
| | 13. | 25468 | 25458 | +10 |
| | 14. | 25568 | 25601 | -33 |
| | 15. | 26059 | 26143 | -84 |
| | 16. | 25493 | 25530 | -37 |
| | 17. | 24961 | 24916 | +45 |
| | 18. | 22814 | 22851 | -37 |
| | 19. | 24415 | 24419 | -4 |
| | 20. | 24890 | 24882 | +8 |
| III | 21. | 34860 | 34723 | +137 |
| | 22. | 35569 | 35295 | +274 |
| | 23. | 34986 | 34982 | +4 |
| | 24. | 36662 | 36582 | +80 |
| | 25. | 33530 | 33528 | +2 |
| | 26. | 34103 | 34036 | +67 |
| | 27. | 33611 | 33589 | +22 |
| | 28. | 32972 | 33051 | -79 |
| | 29. | 35472 | 35536 | -64 |
| | 30. | 32222 | 32563 | -341 |
| | 31. | 31637 | 31749 | -112 |
| | 32. | 32262 | 32341 | -79 |
| IV | 33. | 19800 | 19749 | +51 |
| | 34. | 22086 | 22052 | +34 |
| | 35. | 21038 | 20978 | +60 |
| | 36. | 17899 | 17940 | -41 |
| | 37. | 17208 | 17184 | +24 |
| | 38. | 19602 | 19569 | +33 |
| | 39. | 22180 | 22084 | +96 |
| | 40. | 21756 | 21745 | +11 |
| | 41. | 21949 | 21951 | -2 |
| V | 42. | 24963 | 24960 | +3 |
| | 43. | 24125 | 24041 | +84 |
| | 44. | 26079 | 26004 | +75 |
| | 45. | 24419 | 24488 | -69 |
| | 46. | 23649 | 23676 | -27 |
| | 47. | 23837 | 23838 | -1 |
| | 48. | 23226 | 23249 | -23 |
| | 49. | 25065 | 25094 | -29 |
| VI | 50. | 28684 | 28698 | -14 |
| | 51. | 30373 | 30281 | +92 |
| | 52. | 28743 | 28684 | +59 |
| | 53. | 28487 | 28521 | -34 |
| | Mean: | 27112 | 27106 | +6 |

Table D-IV

**PAIRED COMPARISON OF OXYGEN CONSUMPTION CALCULATED ACCORDING TO HALDANE AND WITH DIRECT MEASUREMENT OF INSPIRED VOLUME.**

| | | ml/min (STPD) | | |
|---|---|---|---|---|
| Subj. | Test No. | Hald. | dir. | diff. |
| I | 1. | 1582 | 1553 | +29 |
| | 2. | 1518 | 1525 | - 7 |
| | 3. | 1571 | 1547 | +24 |
| | 4. | 1417 | 1445 | -28 |
| | 5. | 1475 | 1465 | +10 |
| | 6. | 1408 | 1418 | -10 |
| | 7. | 1433 | 1433 | 0 |
| | 8. | 1384 | 1380 | + 4 |
| | 9. | 1402 | 1381 | +21 |
| | 10. | 1660 | 1643 | +17 |
| II | 11. | 1462 | 1469 | - 7 |
| | 12. | 1547 | 1554 | - 7 |
| | 13. | 1582 | 1580 | + 2 |
| | 14. | 1486 | 1493 | - 7 |
| | 15. | 1408 | 1425 | -17 |
| | 16. | 1582 | 1590 | - 8 |
| | 17. | 1434 | 1424 | +10 |
| | 18. | 1405 | 1402 | + 3 |
| | 19. | 1417 | 1418 | - 1 |
| | 20. | 1338 | 1336 | + 2 |
| III | 21. | 2164 | 2180 | -16 |
| | 22. | 2266 | 2289 | -23 |
| | 23. | 2204 | 2276 | -72 |
| | 24. | 2299 | 2312 | -13 |
| | 25. | 2193 | 2211 | -18 |
| | 26. | 2300 | 2296 | + 4 |
| | 27. | 2123 | 2109 | +14 |
| | 28. | 2147 | 2147 | 0 |
| | 29. | 2161 | 2144 | +17 |
| | 30. | 2266 | 2265 | + 1 |
| | 31. | 2329 | 2272 | +57 |
| | 32. | 2287 | 2257 | +30 |
| IV | 33. | 1108 | 1097 | +11 |
| | 34. | 1307 | 1300 | + 7 |
| | 35. | 1270 | 1258 | +12 |
| | 36. | 1203 | 1212 | - 9 |
| | 37. | 1129 | 1124 | + 5 |
| | 38. | 1109 | 1102 | + 7 |
| | 39. | 1250 | 1230 | +20 |
| | 40. | 1169 | 1166 | + 3 |
| | 41. | 1218 | 1219 | - 1 |
| V | 42. | 1473 | 1455 | +18 |
| | 43. | 1484 | 1468 | +16 |
| | 44. | 1427 | 1442 | -15 |
| | 45. | 1375 | 1381 | - 6 |
| | 46. | 1379 | 1380 | - 1 |
| | 47. | 1376 | 1380 | - 4 |
| | 48. | 1410 | 1416 | - 6 |
| | 49. | 1399 | 1399 | 0 |
| VI | 50. | 1369 | 1372 | - 3 |
| | 51. | 1365 | 1346 | +19 |
| | 52. | 1342 | 1329 | +13 |
| | 53. | 1401 | 1408 | - 7 |
| | Mean: | 1581 | 1580 | + 1 |

Table D-V

EXPIRED $N_2$ FRACTION

| Subj. | Test No. | | Subj. | Test No. | |
|---|---|---|---|---|---|
| I | 1. | .7920 | | 28. | .7943 |
| | 2. | .7936 | | 29. | .7942 |
| | 3. | .7923 | | 30. | .7938 |
| | 4. | .7949 | | 31. | .7955 |
| | 5. | .7914 | | 32. | .7951 |
| | 6. | .7931 | IV | 33. | .7885 |
| | 7. | .7919 | | 34. | .7901 |
| | 8. | .7939 | | 35. | .7903 |
| | 9. | .7932 | | 36. | .7930 |
| | 10. | .7942 | | 37. | .7936 |
| II | 11. | .7943 | | 38. | .7901 |
| | 12. | .7939 | | 39. | .7896 |
| | 13. | .7941 | | 40. | .7889 |
| | 14. | .7954 | | 41. | .7904 |
| | 15. | .7910 | V | 42. | .7905 |
| | 16. | .7950 | | 43. | .7933 |
| | 17. | .7932 | | 44. | .7918 |
| | 18. | .7961 | | 45. | .7947 |
| | 19. | .7925 | | 46. | .7932 |
| | 20. | .7895 | | 47. | .7932 |
| III | 21. | .7930 | | 48. | .7941 |
| | 22. | .7952 | | 49. | .7915 |
| | 23. | .7945 | VI | 50. | .7909 |
| | 24. | .7921 | | 51. | .7895 |
| | 25. | .7916 | | 52. | .7893 |
| | 26. | .7923 | | 53. | .7908 |
| | 27. | .7956 | | Mean: | .7926 |

Table D-VI

EXPIRED VENTILATION ( 1/min STPD)

| Subj. | Test No. | |
|---|---|---|
| I | 1. | 31.633 |
| | 2. | 26.409 |
| | 3. | 27.334 |
| | 4. | 26.920 |
| | 5. | 28.285 |
| | 6. | 28.021 |
| | 7. | 27.724 |
| | 8. | 29.955 |
| | 9. | 29.049 |
| | 10. | 29.274 |
| II | 11. | 23.560 |
| | 12. | 24.880 |
| | 13. | 25.346 |
| | 14. | 25.416 |
| | 15. | 26.039 |
| | 16. | 25.342 |
| | 17. | 24.870 |
| | 18. | 22.648 |
| | 19. | 24.348 |
| | 20. | 24.916 |
| III | 21. | 34.742 |
| | 22. | 35.350 |
| | 23. | 34.802 |
| | 24. | 36.578 |
| | 25. | 33.476 |
| | 26. | 34.018 |
| | 27. | 33.387 |
| | 28. | 32.805 |
| | 29. | 35.299 |
| | 30. | 32.081 |
| | 31. | 31.430 |
| | 32. | 32.066 |
| IV | 33. | 19.846 |
| | 34. | 22.092 |
| | 35. | 21.038 |
| | 36. | 17.838 |
| | 37. | 17.136 |
| | 38. | 19.608 |
| | 39. | 22.200 |
| | 40. | 21.795 |
| | 41. | 21.947 |
| V | 42. | 24.956 |
| | 43. | 24.034 |
| | 44. | 26.030 |
| | 45. | 24.283 |
| | 46. | 23.563 |
| | 47. | 23.749 |
| | 48. | 23.115 |
| | 49. | 25.027 |
| VI | 50. | 28.661 |
| | 51. | 30.403 |
| | 52. | 28.780 |
| | 53. | 28.470 |
| | Mean: | 27.030 |

## E. THE USE OF THE FORCED-OSCILLATION METHOD TO DETERMINE TOTAL RESPIRATORY CONDUCTANCE IN HEALTHY SUBJECTS AND PULMONARY PATIENTS

Preliminary results of the use of sine-wave forcing superimposed on the respiratory pattern as a means of estimating total respiratory resistance (TRR) or its reciprocal, total respiratory conductance (TRC), were presented in section IIA of the Final Report dated February 1970 under contract NAS 9-7009.

The following report describes results obtained with this method on 212 subjects who had all performed the usual pulmonary function tests used in this laboratory, thus providing an opportunity to compare the forced-oscillation (FO) method with other indices of obstructive impairment, such as maximal mid-expiratory flow (MMEF) and forced expiratory volume in one second ($FEV_1$).

Procedure:

Measurements of TRC were made as described previously (NAS 9-7009 Rep., February 1970). More recently, the forced oscillations are generated by a constant volume, variable frequency pneumatic pump specially designed for this purpose, instead of the low-frequency loudspeaker (Acoustic Research, Inc.) used previously. The pump consists of twin pistons with sliding diaphragms which operate in phase in two cylinders positioned opposite each other at right angles to the main breathing tube (Fig. E-1). The stroke volume is adjustable between 15 and 45 ml, and the frequency between 2 and 17 Hz . The advantage of the pump over the loudspeaker is that its stroke volume does not vary with the changing impedance load during the respiratory cycle. A constant bias flow of 0.5 L/sec is drawn through the system by suction line to minimize rebreathing. A measurement of TRC (Fig. E-2) is usually obtained in less than 30 seconds by rotating a template on the screen of the oscilloscope to cover the longitudinal axis of the flow/pressure loop after reducing its diameter to an approximately straight line at resonant frequency by varying the rate of oscillation. Readings were taken as close to the normal end-tidal levels as possible. The results of this test are given as total respiratory conductance (TRC) in L/sec:cm $H_2O$ rather than total respiratory resistance,

because the former is linearly related to lung volume, whereas the latter is not.

Subjects:

The group of 212 subjects, enumerated in Table E-I, consisted of 44 children and 64 adult volunteers who had no history of pulmonary disease nor abnormalities in the routine pulmonary function tests. Only seven pediatric patients were studied with clinically and functionally manifest obstructive disease. Of the 97 adult patients (Table E-II), 33 were classified as non-obstructive. These were suffering from restrictive impairment and/or interstitial pulmonary disorders. All patients in the obstructive group had an MMEF/VC ratio of less than 0.5. In 48 of the adult patients with obstructive disease measurements of TRC and MMEF were made both before and after administration of bronchodilator (Isuprel aerosol). Individual measurements on all subjects are given in the Appendix E-I, while the results of all statistical analysis, namely means and standard deviations for each item measured and correlations between items for each group of subjects, are shown in Appendix E-II with tests for significance.

Results:

In order to determine whether the measurement of total respiratory conductance (TRC) by the forced-oscillation method is valid as a discriminating test for obstructive impairment, a comparison was made with the results of tests for the same purpose frequently used in pulmonary function laboratories, namely maximal mid-expiratory flow (MMEF) measured on the flow-volume loop and the forced expired volume in one second ($FEV_1$) obtained from the fast vital capacity on a spirometer. The absolute values of all three measurements, compared in Table E-III, are affected not only by the impedance of the airways but also by the size of the individual's lungs. Therefore, it is useful to relate each measurement to the appropriate lung volume, if one wishes to compare individuals or different groups. For this reason, it is customary to relate the MMEF and the $FEV_1$ to the vital capacity (VC) and by the same token, we have related TRC to the functional residual capacity (FRC). Table E-III presents mean values for normal children and adults and the two groups of adult patients. Among the adults, MMEF, $FEV_1$,

and TRC are highest in the normals, slightly lower in the non-obstructive patients, but substantially lower in the obstructive cases. For the normal children, MMEF, $FEV_1$, and TRC are comparable to the values seen in the obstructive adults. However, when each of the measurements is adjusted for the appropriate lung volumes, the normal children are slightly superior to the normal adults. This would suggest that the dimensions of the airways in children are in good proportion to the size of their lungs.

In order to assess the effectiveness of the forced-oscillation method in discriminating between normal and pathological cases, as compared to MMEF and $FEV_1$, the statistical significance of the difference between 64 normal adults and 64 patients with established obstructive disease was calculated for all three methods with their respective volume adjustments using the student t-test. The results with t- and p-values in descending order of magnitude are given in Table E-IV. It is not surprizing that MMEF/FVC and MMEF are at the top of the list, because this test was used in the first place to separate the obstructive from the normal group. However, TRC also shows the same high level of significance ($p < .001$), although the t-value is not quite as large as for MMEF and $FEV_1$. The results are even better using TRC/FRC. It is apparent that the significance of the difference and thus the discriminatory power improves for all three methods, when the volume adjustment is made. The comparison between normal and obstructive children is somewhat lopsided with only seven patients to 44 normals (Table E-IV, below). In the t-test for differences TRC ranks even higher than in the adult group, being nearly as good as MMEF/FVC and better than $FEV_1/VC$. It is noteworthy here that the difference in $FEV_1$ is barely significant in the children, whereas for $FEV_1/VC$ it is highly significant. Apparently the adjustment for volume is even more important in children with large differences in size.

In as much as TRC is apparently equivalent to MMEF and $FEV_1$ as a test for detecting obstructive impairment, one might expect to find a good statistical correlation between TRC and the other two methods. Correlation coefficients (r) and their significance (p-values) were computed for TRC versus MMEF and $FEV_1$ as actually measured and with adjustment for volume (Table E-V). In the adults with obstructive lung disease, there was a highly significant correlation between TRC and both of the other methods ($p < .0005$). In the normal adults, on the other hand, the correlation between TRC and

MMEF was not significant, but highly significant with $FEV_1$ when lung volumes were not taken into account. However, when each of the measurements is related to the appropriate lung volume (TRC/FRC, MMEF/VC, and $FEV_1$/VC), neither of the correlations is significant. This suggests that the significant correlation between TRC and $FEV_1$ is strongly biased by the variance in lung volume in the normal adults. Looking again at the same correlations in the adult obstructive patients, they are highly significant, regardless of whether the data are adjusted for volume or not. The reason for this may be because TRC has a good correlation with FRC in normal adults ($r = .436$, $p < .0005$), but there is no correlation at all between the two in patients with obstructive disease ($r = .03$, not significant). Obstructive disease, particularly pulmonary emphysema, is characterized by an FRC that is grossly enlarged relative to total lung capacity.

It is noteworthy that the highest correlations were found in normal children between TRC, and MMEF and $FEV_1$, respectively; but, as in the normal adults, the correlation is less striking for TRC/FRC versus MMEF/VC and is not significant for TRC/FRC versus $FEV_1$/VC, because the differences in body size and lung volumes were even greater among the children than in the adults. These observations tend to confirm the contention that TRC as well as MMEF and $FEV_1$ are more specific as criteria for obstructive impairment when differences in lung volume are taken into account, except in cases with emphysema where normal lung volume relationships are disturbed.

The ability of the FO method to detect changes in airway impedance was tested further in a series where TRC and MMEF were measured before and after administration of bronchodilator in aerosol form (Isuprel 1:200 solution by vaporizer) to 48 patients who were responsive to this therapy. Fig. E-1 shows the difference in MMEF before and after bronchodilator which was statistically highly significant ($t = 7.17$, $p < .001$) compared to the difference in TRC, also highly significant ($t = 5.0$, $p < .001$). Thus it appears that the results obtained with the FO method compare very favorably with one of the most sensitive tests for changes in airway impedance. The simplicity of the procedure and independence of effort and motivation on the part of the subject make the FO method more attractive, particularly for pediatric use and for screening purposes.

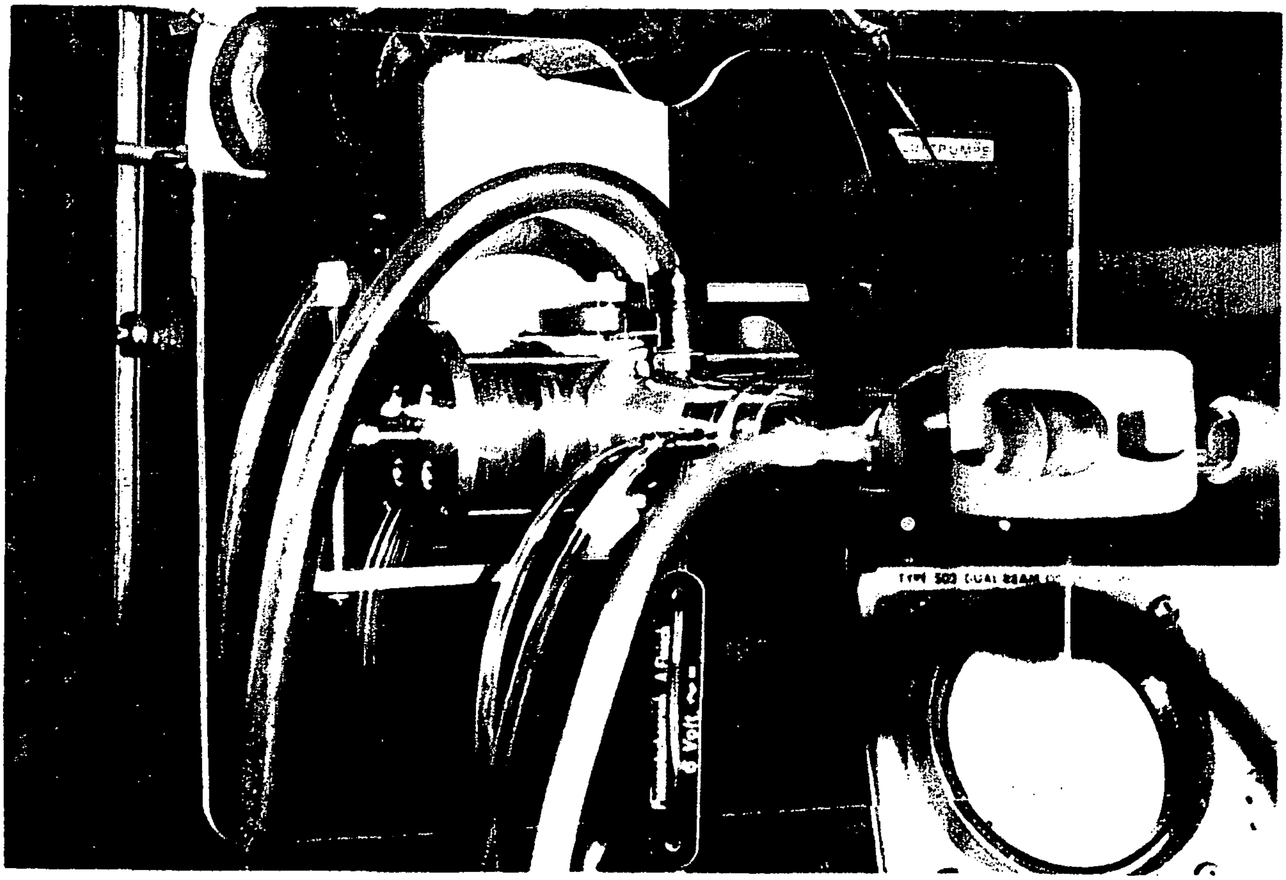

Fig. E-1. Apparatus used in forced-oscillation method for total respiratory conductance with dual sliding membrane pump and mouthpiece

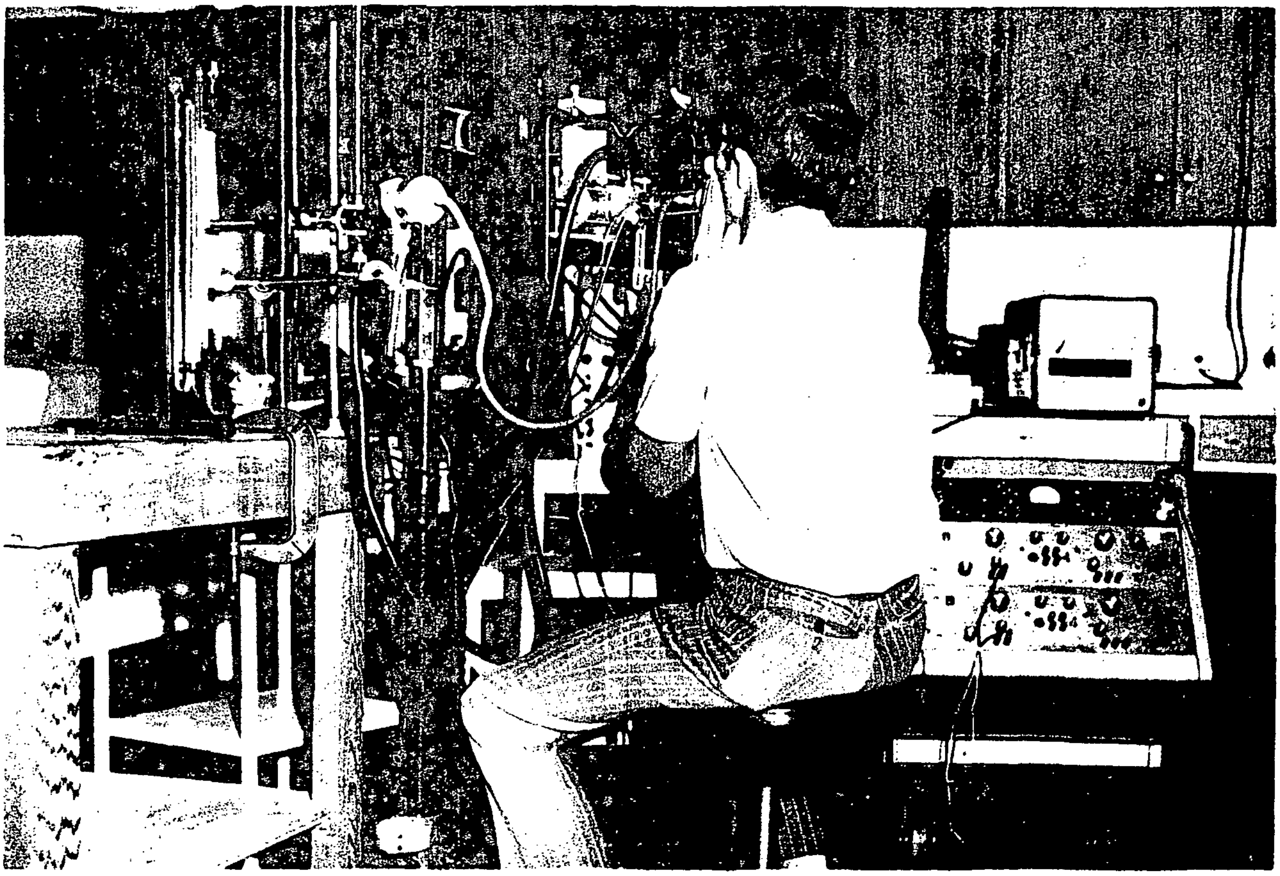

Fig. E-2. Measuring total respiratory conductance by the forced-oscillation method. Subject holds his cheeks to avoid artifacts.

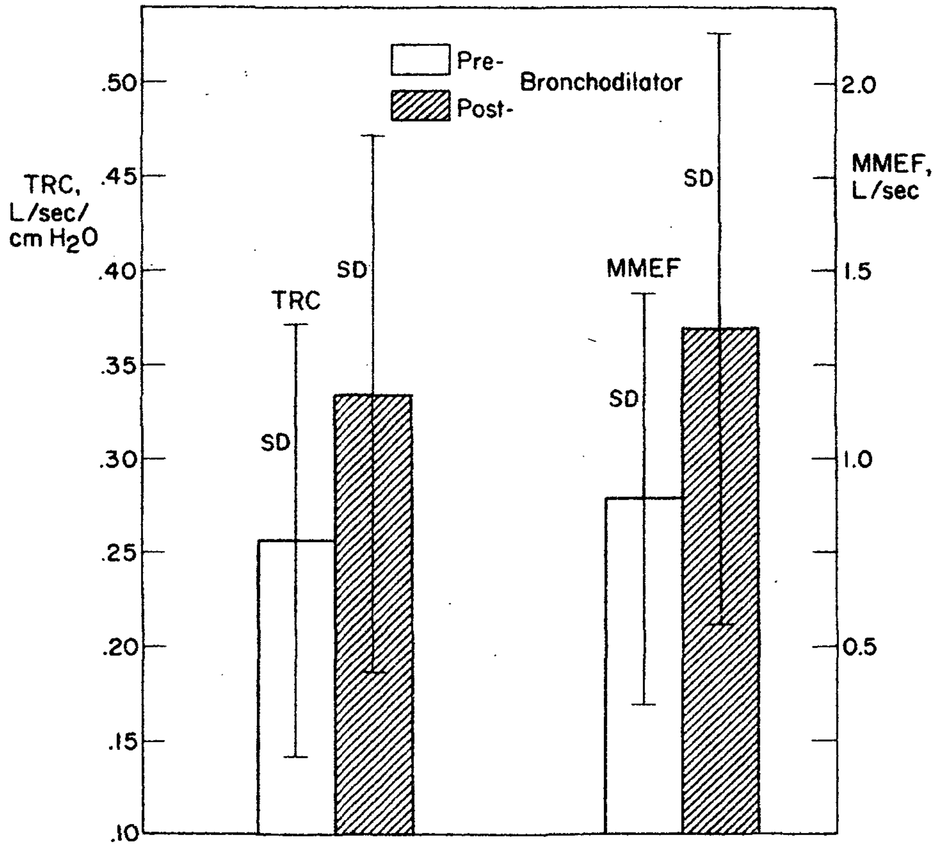


Fig. E-3. Mean values for total respiratory conductance by forced-oscillation (left) and maximal mid-expiratory flow (right) on 48 patients with chronic obstructive disease before and after (shaded) bronchodilator by inhalation. One standard deviation is shown for each column.

Table E-I. Size and age distribution of groups

Children

| Normals | | Patients | |
|---|---|---|---|
| Age | No. | Age | No. |
| 6-9 | 26 | 6-9 | 4 |
| 10-12 | 8 | 10-12 | 3 |
| 13-16 | 10 | 13-16 | 0 |
| Total | 44 | Total | 7 |

Adults

| Normals | | Patients | |
|---|---|---|---|
| Age | No. | Age | No. |
| 17-19 | 2 | 17-19 | 1 |
| 20-29 | 12 | 20-29 | 4 |
| 30-39 | 13 | 30-39 | 5 |
| 40-49 | 12 | 40-49 | 22 |
| 50-59 | 11 | 50-59 | 21 |
| 60-69 | 10 | 60-69 | 33 |
| 70-79 | 4 | 70-79 | 11 |
| Total | 64 | Total | 97 |

Table E-II. Classification of adult patient group

| Non-Obstructive | | Obstructive | |
|---|---|---|---|
| Age | No. | Age | No. |
| 17-19 | 0 | 17-19 | 1 |
| 20-29 | 4 | 20-29 | 0 |
| 30-39 | 2 | 30-39 | 3 |
| 40-49 | 10 | 40-49 | 12 |
| 50-59 | 8 | 50-59 | 13 |
| 60-69 | 7 | 60-69 | 26 |
| 70-79 | 2 | 70-79 | 9 |
| Total | 33 | Total | 64 |

Table E-III.

| | | CHILDREN | ADULTS | | |
|---|---|---|---|---|---|
| | | Normal (n = 44) | Normal (n = 64) | Non-Obstructive (n = 33) | Obstructive (n = 64) |
| MMEF (L/sec) | Mean | 2.616 | 4.028 | 2.859 | 0.887 |
| | SD | 1.139 | 1.407 | 1.245 | 0.564 |
| MMEF/ VC (L/sec/L) | Mean | 1.214 | 0.922 | 0.811 | 0.290 |
| | SD | 0.376 | 0.254 | 0.239 | 0.121 |
| $FEV_1$ (L) | Mean | 1.848 | 3.137 | 2.405 | 1.484 |
| | SD | 0.758 | 0.948 | 0.735 | 0.693 |
| $FEV_1/VC$ (L/L) | Mean | 0.794 | 0.726 | 0.687 | 0.469 |
| | SD | 0.083 | 0.096 | 0.103 | 0.125 |
| TRC (L/sec/ cm $H_2O$) | Mean | 0.226 | 0.470 | 0.408 | 0.253 |
| | SD | 0.104 | 0.191 | 0.198 | 0.115 |
| TRC/FRC (L/sec/ cm $H_2O$/L) | Mean | 0.167 | 0.140 | 0.135 | 0.064 |
| | SD | 0.047 | 0.052 | 0.070 | 0.033 |

Mean values and standard deviations for maximal mid-expiratory flow (MMEF), forced expiratory volume in one second ($FEV_1$), and total respiratory conductance (TRC) for normal children and adults, and non-obstructive and obstructive adult patients. VC is vital capacity and FRC functional residual capacity.

Table E-IV.

Above: Significance tests (student's t) for difference between normal adults (64) and obstructive adult patients (64) for MMEF, $FEV_1$, and TRC with and without adjustment for volume, VC, or FRC, respectively (for abbreviations see Table E-III)

Below: The same as above for 44 normal children and 7 obstructive young patients

Normal Adults (n = 64) vs Obstructive Adult Patients (n = 64)

| | t | p |
|---|---|---|
| MMEF/VC | 17.8 | $p < .001$ |
| MMEF | 16.5 | $p < .001$ |
| $FEV_1$/VC | 13.0 | $p < .001$ |
| $FEV_1$ | 11.2 | $p < .001$ |
| TRC/FRC | 9.6 | $p < .001$ |
| TRC | 7.7 | $p < .001$ |

Normal Children (n = 44) vs Pediatric Patients (n = 7)

| | t | p |
|---|---|---|
| MMEF/VC | 8.5 | $p < .001$ |
| TRC | 6.0 | $p < .001$ |
| $FEV_1$/VC | 5.9 | $p < .001$ |
| TRC/FRC | 5.3 | $p < .001$ |
| MMEF | 3.5 | $p < .01$ |
| $FEV_1$ | 2.4 | $p < .05$ |

Table E-V

| | CHILDREN | ADULTS | | |
|---|---|---|---|---|
| | Normal (n = 44) | Normal (n = 64) | Non-Obstructive (n = 33) | Obstructive (n = 64) |
| | r | r | r | r |
| TRC vs MMEF | 0.773 ($p < .0005$) | 0.160 ( NS ) | 0.221 ( NS ) | 0.443 ($p < .0005$) |
| TRC vs $FEV_1$ | 0.767 ($p < .0005$) | 0.472 ($p < .0005$) | 0.211 ( NS ) | 0.568 ($p < .0005$) |
| TRC/FRC vs MMEF/VC | 0.427 ($p < .0005$) | -0.109 ( NS ) | 0.143 ( NS ) | 0.337 ($p < .005$) |
| TRC/FRC vs $FEV_1$/VC | 0.184 ( NS ) | 0.209 ( NS ) | 0.258 ( NS ) | 0.554 ($p < .0005$) |

Correlation coefficients (r) and significance levels for TRC measured by forced-oscillation method with MMEF and with $FEV_1$ in four groups of subjects as indicated. Above without and below with volume adjustment. NS: not significant.

## Appendix E-I

Pulmonary Function Measurements
and
Forced Oscillation Data

Normal Children:

| Subj.# | Age | $FEV_1$ (L) | MMEF (L/sec) | FRC (L) | VC (L) | FVC (L) | Res. Freq. (Hz) | TPC (L/sec/cm $H_2O$) |
|---|---|---|---|---|---|---|---|---|
| 1 | 7 | 1.64 | 2.02 | 1.10 | 1.84 | 1.69 | 4.70 | 0.1951 |
| 2 | 8 | 1.40 | 2.04 | 1.22 | 2.03 | 1.55 | 4.73 | 0.1781 |
| 3 | 12 | 2.56 | 3.58 | 1.67 | 3.16 | 3.22 | 5.03 | 0.2217 |
| 4 | 9 | 1.55 | 1.91 | 1.46 | 1.94 | 1.93 | 4.97 | 0.2698 |
| 5 | 13 | 2.32 | 1.96 | 2.01 | 2.70 | 2.60 | 4.99 | 0.2698 |
| 6 | 10 | 1.79 | 2.02 | 1.28 | 2.33 | -- | 5.05 | 0.2698 |
| 7 | 6 | 1.03 | 1.78 | 1.16 | 1.18 | 1.04 | 4.77 | 0.1781 |
| 8 | 9 | 1.73 | 1.82 | 1.09 | 2.16 | 2.24 | 5.13 | 0.1147 |
| 9 | 7 | 1.29 | 1.86 | 1.12 | 1.74 | 1.37 | 5.27 | 0.0997 |
| 10 | 14 | 2.95 | 4.50 | 2.22 | 3.51 | 3.37 | 4.32 | 0.3730 |
| 11 | 9 | 1.70 | 2.40 | 1.39 | 2.18 | 2.13 | 4.92 | 0.1223 |
| 12 | 6 | 1.34 | 1.50 | 1.09 | 1.65 | 1.60 | 4.67 | 0.1535 |
| 13 | 8 | 1.75 | 2.50 | 1.23 | 2.11 | 2.35 | 4.42 | 0.2038 |
| 14 | 14 | 3.27 | 4.00 | 1.82 | 4.19 | 4.07 | 4.27 | 0.3125 |
| 15 | 10 | 2.11 | 2.36 | 1.57 | 2.51 | 2.49 | 4.27 | 0.2499 |
| 16 | 15 | 3.38 | 3.41 | 2.51 | 3.88 | 4.19 | 4.72 | 0.4000 |
| 17 | 14 | 3.25 | 3.95 | 2.44 | 3.73 | 3.28 | 4.75 | 0.3239 |
| 18 | 6 | 0.84 | 2.00 | 0.81 | 1.22 | 1.13 | 4.78 | 0.1781 |
| 19 | 6 | -- | 1.96 | 0.82 | 1.20 | 1.13 | 4.62 | 0.2127 |
| 20 | 13 | 1.88 | 2.82 | 1.37 | 2.26 | 2.49 | 4.60 | 0.2598 |
| 21 | 13 | 2.26 | 2.27 | 2.10 | 3.28 | 3.35 | 5.23 | 0.1616 |
| 22 | 10 | 1.81 | 2.57 | 1.71 | 2.92 | 2.66 | 4.85 | 0.1865 |
| 23 | 8 | 1.98 | 4.50 | 1.12 | 2.41 | 2.31 | 4.61 | 0.3356 |
| 24 | 10 | 1.87 | 3.30 | 1.09 | 2.15 | 1.98 | 4.61 | 0.2217 |
| 25 | 8 | 1.36 | 1.50 | 1.01 | 2.03 | 2.01 | 4.21 | 0.2403 |
| 26 | 13 | 2.13 | 3.09 | 1.32 | 3.09 | 3.31 | 4.67 | 0.1616 |
| 27 | 9 | 1.17 | 1.68 | 1.26 | 1.63 | 1.73 | 5.05 | 0.1456 |
| 28 | 6 | 0.68 | 1.30 | 0.98 | 1.31 | 1.45 | 4.99 | 0.1535 |
| 29 | 7 | 1.29 | 2.20 | 0.85 | 1.70 | 1.49 | 5.15 | 0.1616 |
| 30 | 7 | 1.15 | 2.74 | 0.77 | 1.38 | 1.32 | 4.97 | 0.0778 |
| 31 | 9 | 1.91 | 3.50 | 1.02 | 2.33 | 2.51 | 4.97 | 0.2309 |
| 32 | 12 | 2.10 | 4.84 | 1.65 | 2.69 | 2.64 | 5.43 | 0.3356 |
| 33 | 9 | 1.90 | 2.75 | 1.78 | 2.47 | 2.56 | 4.78 | 0.2801 |
| 34 | 10 | 1.75 | 3.00 | 1.09 | 1.99 | 1.75 | 4.91 | 0.1616 |
| 35 | 15 | 3.74 | 4.40 | 2.54 | 4.74 | 4.60 | 4.81 | 0.3356 |
| 36 | 7 | 0.97 | 0.88 | 0.91 | 1.17 | 1.21 | 4.66 | 0.1535 |
| 37 | 6 | 1.12 | 1.62 | 0.66 | 1.36 | 1.23 | 4.95 | 0.1147 |
| 38 | 8 | 1.52 | 1.32 | 1.36 | 1.88 | 1.92 | 4.54 | 0.2403 |
| 39 | 7 | 1.36 | 1.50 | 1.10 | 1.70 | 1.76 | 4.54 | 0.1951 |
| 40 | 7 | 1.14 | 2.35 | 0.72 | 1.32 | 1.34 | 4.33 | 0.1781 |
| 41 | 6 | 1.36 | 2.10 | 0.97 | 1.43 | 1.34 | 5.02 | 0.2038 |
| 42 | 7 | 1.34 | 1.71 | 0.87 | 1.61 | 1.60 | 4.77 | 0.1456 |
| 43 | 15 | 3.76 | 6.50 | 3.37 | 5.22 | 5.13 | 4.14 | 0.6928 |
| 44 | 12 | 2.03 | 3.09 | 1.39 | 2.21 | 2.30 | 4.58 | 0.2309 |

Pediatric Patients:

| Subj. # | Age | $FEV_1$ (L) | MMEF (L/sec) | FRC (L) | VC (L) | FVC (L) | Res. Freq. (Hz) | TPC (L/sec/cm $H_2O$) |
|---|---|---|---|---|---|---|---|---|
| 1 | 7 | 1.33 | 1.52 | 1.26 | 2.01 | 1.90 | 5.15 | 0.1300 |
| 2 | 6 | 0.85 | 0.77 | 1.59 | 1.42 | 1.53 | 4.95 | 0.0778 |
| 3 | 10 | 1.46 | 1.40 | 1.92 | 2.28 | 2.35 | 5.43 | 0.1223 |
| 4 | 7 | 0.86 | 0.77 | 1.12 | 1.49 | 1.27 | 5.02 | 0.0705 |
| 5 | 9 | 0.52 | 0.32 | 1.56 | 1.01 | 0.81 | 5.23 | 0.1535 |
| 6 | 10 | 1.43 | 1.30 | 1.71 | 2.39 | 2.31 | 4.75 | 0.1223 |
| 7 | 12 | 1.57 | 1.47 | 2.29 | 2.49 | 2.33 | 4.93 | 0.0924 |

Normal Adults:

| Subj. # | Age | $FEV_1$ (L) | MMEF (L/sec) | FRC (L) | VC (L) | FVC (L) | Res. Freq. (Hz) | TPC (L/sec/cm $H_2O$) |
|---|---|---|---|---|---|---|---|---|
| 1 | 46 | 3.77 | 5.48 | 4.10 | 5.38 | 4.69 | 5.00 | 0.5308 |
| 2 | 31 | 4.87 | 3.63 | 4.56 | 6.67 | 6.48 | 5.40 | 0.9424 |
| 3 | 30 | 3.29 | 5.43 | 3.78 | 5.22 | 5.05 | 4.60 | 0.4142 |
| 4 | 50 | 1.83 | 3.25 | 4.52 | 5.38 | 5.87 | 4.95 | 0.4602 |
| 5 | 57 | 3.55 | 2.58 | 5.03 | 5.15 | 5.27 | 4.70 | 0.5506 |
| 6 | 71 | 1.91 | 2.83 | 3.75 | 2.90 | 2.94 | 4.61 | 0.2499 |
| 7 | 25 | 3.32 | 4.96 | 2.82 | 4.26 | 4.81 | 4.95 | 0.3602 |
| 8 | 21 | 4.24 | 5.04 | 3.76 | 5.17 | 5.39 | 4.97 | 0.5712 |
| 9 | 25 | 3.65 | 3.13 | 4.38 | 6.09 | 5.94 | 4.57 | 0.5308 |
| 10 | 20 | 4.92 | 6.08 | 4.52 | 5.79 | 5.83 | 5.03 | 0.4602 |
| 11 | 64 | 2.31 | 2.08 | 3.90 | 3.26 | 3.19 | 4.72 | 0.3602 |
| 12 | 67 | 2.23 | 3.09 | 3.79 | 3.85 | 4.25 | 5.25 | 0.8984 |
| 13 | 75 | 1.39 | 1.45 | 2.49 | 1.80 | 1.87 | 4.46 | 0.5930 |
| 14 | 54 | 2.03 | 3.09 | 2.80 | 2.63 | 2.68 | 4.28 | 0.3863 |
| 15 | 33 | 4.54 | 4.64 | 3.35 | 6.14 | 5.44 | 5.10 | 0.6657 |
| 16 | 59 | 2.80 | 4.27 | 3.39 | 4.38 | 4.09 | 4.28 | 0.5506 |
| 17 | 37 | 2.86 | 3.35 | 4.40 | 5.01 | 4.46 | 4.42 | 0.4767 |
| 18 | 49 | 3.24 | 3.90 | 3.31 | 4.99 | 4.97 | 4.32 | 0.6928 |
| 19 | 49 | 3.53 | 5.27 | 2.92 | 4.90 | 4.97 | 4.79 | 0.2698 |
| 20 | 57 | 1.88 | 1.74 | 2.39 | 2.68 | 2.75 | 4.68 | 0.2309 |
| 21 | 59 | 1.88 | 2.09 | 2.47 | 2.73 | 2.98 | 4.85 | 0.2403 |
| 22 | 60 | 2.84 | 4.00 | 3.93 | 4.51 | 4.49 | 5.23 | 0.1865 |
| 23 | 62 | 2.33 | 4.30 | 3.19 | 3.64 | 3.54 | 4.59 | 0.3730 |
| 24 | 17 | 4.11 | 5.18 | 2.41 | 5.41 | 5.45 | 5.14 | 0.2403 |
| 25 | 72 | 3.51 | 3.50 | 3.01 | 4.74 | 5.41 | 4.45 | 0.7216 |
| 26 | 26 | 2.89 | 4.20 | 2.37 | 3.66 | 3.47 | 4.52 | 0.4290 |
| 27 | 20 | 3.01 | 4.20 | 2.84 | 3.34 | 4.17 | 4.57 | 0.4000 |
| 28 | 28 | 3.34 | 5.00 | 2.90 | 4.18 | 4.12 | 4.52 | 0.4602 |
| 29 | 61 | 2.35 | 3.60 | 3.08 | 3.79 | 3.67 | 4.77 | 0.2127 |
| 30 | 39 | 4.10 | 6.90 | 3.96 | 5.70 | 5.62 | 5.15 | 0.5712 |
| 31 | 26 | 5.54 | 8.50 | 3.34 | 6.76 | 6.48 | 4.23 | 0.5308 |
| 32 | 50 | 3.15 | 6.11 | 3.95 | 4.25 | 4.48 | 4.49 | 0.3356 |
| 33 | 36 | 4.05 | 6.10 | 3.45 | 5.62 | 5.63 | 4.98 | 0.3014 |
| 34 | 55 | 2.19 | 4.22 | 2.96 | 2.85 | 3.21 | 4.28 | 0.3602 |
| 35 | 46 | 1.96 | 2.05 | 2.99 | 2.80 | 2.80 | -- | -- |
| 36 | 63 | 3.16 | 3.86 | 3.78 | 4.21 | 4.36 | 4.43 | 0.3239 |
| 37 | 37 | 4.48 | 4.73 | 3.85 | 6.22 | 6.15 | 4.60 | 0.3356 |
| 38 | 49 | 2.58 | 3.70 | 1.95 | 3.07 | 3.14 | 4.33 | 0.4290 |
| 39 | 22 | 2.64 | 2.95 | 1.95 | 3.47 | 3.35 | 4.26 | 0.3125 |
| 40 | 61 | 3.15 | 5.86 | 3.44 | 3.84 | 4.11 | 4.08 | 0.5712 |
| 41 | 40 | 4.70 | 4.77 | 5.87 | 6.18 | 6.25 | 4.64 | 0.8201 |

Normal Adults (cont.):

| Subj.# | Age | $FEV_1$ (L) | MMEF (L/sec) | FRC (L) | VC (L) | FVC (L) | Res.Freq. (Hz) | TPC (L/sec/cm $H_2O$) |
|---|---|---|---|---|---|---|---|---|
| 42 | 18 | 2.80 | 5.09 | 3.94 | 5.99 | 5.99 | 4.74 | 0.5506 |
| 43 | 59 | 3.32 | 2.82 | 4.50 | 4.55 | 4.48 | 4.15 | 0.3602 |
| 44 | 53 | 3.69 | 3.50 | 4.44 | 5.43 | 5.93 | 4.51 | 0.4767 |
| 45 | 43 | 2.03 | 2.73 | 1.91 | 2.57 | 2.55 | 4.30 | 0.3730 |
| 46 | 56 | 2.45 | 3.24 | 3.04 | 3.23 | 3.37 | 4.67 | 0.4290 |
| 47 | 61 | 1.94 | 2.18 | 2.81 | 3.13 | 2.75 | 4.55 | 0.2499 |
| 48 | 65 | 3.01 | 2.82 | 3.91 | 4.36 | 4.44 | 3.68 | 0.8578 |
| 49 | 65 | 2.35 | 2.71 | 2.26 | 3.18 | 3.20 | 4.60 | 0.1300 |
| 50 | 29 | 2.87 | 3.64 | 2.49 | 3.38 | 3.43 | 3.37 | 0.5120 |
| 51 | 25 | 3.50 | 3.65 | 2.71 | 4.43 | 4.53 | 3.87 | 0.4290 |
| 52 | 38 | -- | -- | 3.54 | 4.70 | -- | 4.78 | 0.5308 |
| 53 | 79 | 1.42 | 2.96 | 2.22 | 1.97 | 2.17 | -- | -- |
| 54 | 23 | 3.61 | 5.13 | 3.13 | 3.92 | 4.00 | -- | 0.4602 |
| 55 | 44 | 2.75 | 4.42 | 3.08 | 3.35 | 3.57 | -- | 0.3356 |
| 56 | 32 | 2.69 | 4.00 | 3.18 | 3.40 | 3.64 | -- | 0.3602 |
| 57 | 42 | 3.28 | 3.38 | 3.26 | 4.02 | 3.98 | -- | 0.4940 |
| 58 | 38 | 2.31 | 1.92 | 2.47 | 3.66 | 3.77 | -- | 0.3730 |
| 59 | 47 | 3.05 | 5.25 | 3.44 | 3.96 | 4.04 | -- | 0.2801 |
| 60 | 32 | 3.45 | 5.15 | 3.13 | 4.01 | 4.20 | -- | 0.4602 |
| 61 | 41 | 3.46 | 3.29 | 4.45 | 4.88 | 4.70 | -- | 0.6160 |
| 62 | 35 | 4.06 | 3.65 | 4.40 | 5.56 | 5.22 | -- | 0.6401 |
| 63 | 32 | 5.40 | 7.42 | 4.44 | 7.10 | 6.88 | -- | 0.9900 |
| 64 | 42 | 4.09 | 3.73 | 2.81 | 5.53 | 5.55 | -- | 0.8578 |

Adults With Non-Obstructive Pulmonary Disease:

| Subj.# | Age | $FEV_1$ (L) | MMEF (L/sec) | FRC (L) | VC (L) | FVC (L) | Res.Freq. (Hz) | TPC (L/sec/cm $H_2O$) |
|---|---|---|---|---|---|---|---|---|
| 1 | 59 | 2.06 | 1.92 | 2.90 | 2.90 | 2.81 | 5.20 | 1.1617 |
| 2 | 67 | 2.54 | 2.00 | 3.63 | 3.90 | 3.44 | 4.80 | 0.3014 |
| 3 | 61 | 1.46 | 1.83 | 1.66 | 2.08 | 1.85 | 4.86 | 0.4442 |
| 4 | 55 | 1.90 | 2.17 | 3.29 | 2.71 | 2.68 | 4.61 | 0.4290 |
| 5 | 55 | 1.38 | 1.55 | 2.11 | 1.77 | 2.08 | 4.28 | 0.4442 |
| 6 | 27 | 2.89 | 3.86 | 2.50 | 3.36 | 3.63 | 4.18 | 0.5506 |
| 7 | 48 | 2.08 | 2.80 | 3.80 | 3.15 | 3.42 | 4.52 | 0.3356 |
| 8 | 70 | 1.98 | 1.85 | 3.74 | 3.10 | 3.26 | 4.32 | 0.5506 |
| 9 | 20 | 3.48 | 3.24 | 4.48 | 5.12 | 5.39 | 4.77 | 0.4142 |
| 10 | 36 | 2.48 | 3.00 | 2.72 | 3.88 | 3.93 | 4.33 | 0.3863 |
| 11 | 65 | 3.04 | 4.60 | 4.44 | 4.53 | 3.93 | -- | -- |
| 12 | 36 | 2.61 | 2.73 | 2.69 | 3.73 | 3.94 | 4.90 | 0.1951 |
| 13 | 52 | 1.15 | 1.43 | 3.16 | 2.45 | 2.87 | 4.98 | 0.1865 |
| 14 | 54 | 2.16 | 1.91 | 4.28 | 3.43 | 3.28 | 4.61 | 0.2309 |
| 15 | 43 | 3.68 | 7.18 | 4.22 | 4.18 | 4.49 | 4.60 | 0.4767 |
| 16 | 48 | 1.61 | 1.82 | 1.94 | 2.33 | 2.18 | 4.81 | 0.1456 |
| 17 | 64 | 1.46 | 2.86 | 2.99 | 2.08 | 2.22 | 4.77 | 0.2598 |
| 18 | 60 | 2.10 | 2.24 | 3.34 | 3.09 | 2.63 | 4.62 | 0.5506 |
| 19 | 46 | 3.61 | 3.18 | 3.67 | 5.09 | 4.52 | 4.70 | 0.4290 |
| 20 | 49 | 2.92 | 3.45 | 4.63 | 4.36 | 4.61 | 4.73 | 0.5506 |
| 21 | 48 | 3.26 | 3.33 | 2.94 | 3.97 | 4.35 | 4.72 | 0.1865 |
| 22 | 46 | 3.17 | 2.35 | 3.95 | 4.40 | 4.52 | 3.54 | 0.4290 |
| 23 | 55 | 1.61 | 1.90 | 2.33 | 3.28 | 3.04 | 4.61 | 0.1865 |
| 24 | 62 | 2.12 | 2.75 | 3.97 | 5.17 | 3.55 | 4.23 | -- |
| 25 | 51 | 1.41 | 1.14 | 1.65 | 1.91 | 2.04 | 4.10 | 0.2906 |
| 26 | 63 | 3.34 | 4.45 | 3.61 | 4.84 | 4.71 | 4.00 | 0.6401 |

Adults With Non-Obstructive Pulmonary Disease (cont.):

| Subj. # | Age | $FEV_1$ (L) | MMEF (L/sec) | FRC (L) | VC (L) | FVC (L) | Res. Freq. (Hz) | TPC ($L/sec/cm\ H_2O$) |
|---|---|---|---|---|---|---|---|---|
| 27 | 27 | 2.92 | 3.09 | 3.25 | 3.56 | 3.69 | 3.72 | 0.3125 |
| 28 | 77 | 2.18 | 1.91 | 3.74 | 3.58 | 3.19 | 4.00 | 0.3730 |
| 29 | 42 | 1.47 | 1.55 | 2.16 | 1.99 | 2.04 | 3.59 | 0.2801 |
| 30 | 56 | 2.58 | 4.64 | 4.58 | 4.60 | 4.71 | 4.55 | 0.6657 |
| 31 | 25 | 3.24 | 3.55 | 3.59 | 4.56 | 4.76 | 4.39 | 0.5120 |
| 32 | 44 | 2.42 | 3.87 | 2.70 | 3.51 | 3.91 | 3.58 | 0.4142 |
| 33 | 47 | 3.04 | 4.18 | 1.88 | 3.66 | 3.91 | 4.10 | 0.3125 |

Adults With Obstructive Pulmonary Disease:

| Subj. # | Age | $FEV_1$ (L) | MMEF (L/sec) | FRC (L) | VC (L) | FVC (L) | Res. Freq. (Hz) | TPC ($L/sec/cm\ H_2O$) |
|---|---|---|---|---|---|---|---|---|
| 1 | 78 | 0.76 | 0.30 | 4.80 | 2.54 | 1.78 | -- | 0.1781 |
| 2 | 17 | 1.48 | 0.33 | 3.53 | 3.80 | 3.77 | 5.05 | 0.2906 |
| 3 | 47 | 1.25 | 0.48 | 5.56 | 3.28 | 3.22 | 4.45 | 0.2801 |
| 4 | 70 | 1.76 | 0.87 | 5.23 | 3.38 | 3.52 | 4.62 | 0.3730 |
| 5 | 69 | 0.97 | 0.27 | 3.95 | 2.15 | 1.90 | 4.73 | 0.2403 |
| 6 | 48 | 2.19 | 1.00 | 4.83 | 4.30 | 4.44 | 4.48 | 0.5506 |
| 7 | 43 | 2.63 | 2.10 | 3.62 | 4.31 | 4.09 | 4.80 | 0.3356 |
| 8 | 69 | 1.90 | 0.95 | 3.22 | 3.17 | 3.10 | 5.13 | 0.1951 |
| 9 | 65 | 1.00 | 0.86 | 4.08 | 2.49 | 3.04 | 4.98 | 0.2499 |
| 10 | 37 | 1.01 | 0.45 | 3.69 | 2.53 | 2.89 | 4.82 | 0.1147 |
| 11 | 60 | 1.25 | 0.76 | 4.98 | 2.90 | 3.51 | 4.92 | 0.1781 |
| 12 | 71 | 1.38 | 0.64 | 5.03 | 4.30 | 4.16 | 4.48 | 0.3730 |
| 13 | 69 | 0.92 | 0.50 | 4.80 | 2.42 | 2.27 | 4.25 | 0.0997 |
| 14 | 45 | 2.61 | 2.05 | 3.99 | 4.43 | 4.16 | 4.76 | 0.1535 |
| 15 | 49 | 1.86 | 1.27 | 3.32 | 3.51 | 3.42 | 4.99 | 0.1300 |
| 16 | 62 | 1.50 | 0.58 | 4.56 | 3.58 | 3.78 | -- | -- |
| 17 | 40 | 1.86 | 1.50 | 4.45 | 3.05 | 3.42 | 5.22 | 0.1865 |
| 18 | 69 | 0.71 | 0.28 | 6.05 | 2.72 | 2.82 | 4.47 | 0.1865 |
| 19 | 39 | 0.74 | 0.49 | 3.15 | 1.68 | 1.51 | 4.26 | 0.2038 |
| 20 | 35 | 2.18 | 1.80 | 3.62 | 3.75 | 3.87 | 4.98 | 0.1781 |
| 21 | 48 | 1.05 | 0.43 | 5.05 | 3.01 | -- | 4.33 | 0.2698 |
| 22 | 56 | 0.70 | 0.40 | 5.66 | 3.20 | 2.84 | 4.83 | 0.1456 |
| 23 | 66 | 1.48 | 0.88 | 4.54 | 2.59 | 1.93 | 4.47 | 0.2598 |
| 24 | 74 | 1.64 | 1.30 | 3.05 | 3.04 | 2.85 | 4.80 | 0.2309 |
| 25 | 65 | 2.83 | 1.90 | 5.48 | 5.45 | 4.96 | 5.07 | 0.3863 |
| 26 | 57 | 0.78 | 0.21 | 3.08 | 2.22 | 1.80 | 4.47 | 0.1781 |
| 27 | 66 | 0.59 | 0.27 | 6.10 | 2.03 | 1.89 | 4.21 | 0.1535 |
| 28 | 73 | 1.14 | 0.55 | 4.70 | 2.85 | 2.18 | 4.68 | 0.2309 |
| 29 | 58 | 1.43 | 0.61 | 6.59 | 4.22 | 3.56 | 4.46 | 0.3125 |
| 30 | 66 | 0.62 | 0.23 | 6.61 | 2.37 | 1.52 | 4.78 | 0.0778 |
| 31 | 57 | 2.64 | 1.52 | 5.66 | 5.38 | 5.49 | 4.86 | 0.4142 |
| 32 | 64 | 1.99 | 1.05 | 3.61 | 3.56 | 3.57 | 4.94 | 0.5712 |
| 33 | 47 | 1.34 | 0.91 | 3.72 | 3.73 | 3.92 | 4.94 | 0.2801 |
| 34 | 73 | 0.71 | 0.57 | 3.21 | 1.29 | 1.55 | 4.89 | 0.1456 |
| 35 | 53 | 0.89 | 0.45 | 2.07 | 1.42 | 1.38 | 4.13 | 0.2217 |
| 36 | 65 | 3.09 | 2.19 | 5.09 | 5.94 | 4.78 | 4.75 | 0.4442 |
| 37 | 54 | 2.75 | 2.18 | 4.77 | 4.58 | 4.52 | 4.78 | 0.4142 |
| 38 | 55 | 1.00 | 0.86 | 3.50 | 2.93 | 1.85 | 4.00 | 0.2038 |
| 39 | 65 | 0.65 | 0.25 | 6.25 | 2.70 | 2.38 | 4.24 | 0.2906 |
| 40 | 65 | 1.10 | 0.76 | 5.77 | 2.98 | 2.30 | 4.37 | 0.1377 |

Adults With Obstructive Pulmonary Disease (cont.):

| Subj.# | Age | $FEV_1$ (L) | MMEF (L/sec) | FRC (L) | VC (L) | FVC (L) | Res. Freq. (Hz) | TPC (L/sec/cm $H_2O$) |
|---|---|---|---|---|---|---|---|---|
| 41 | 46 | 1.97 | 1.48 | 2.81 | 2.98 | 3.31 | 4.58 | 0.2217 |
| 42 | 78 | 1.14 | 0.42 | 4.40 | 3.00 | 3.19 | 4.08 | 0.1900 |
| 43 | 53 | 2.55 | 1.55 | 3.10 | 4.04 | 3.81 | 4.00 | 0.2038 |
| 44 | 62 | 2.35 | 1.43 | 3.46 | 4.51 | 4.36 | 4.14 | 0.3239 |
| 45 | 55 | 1.30 | 0.81 | 4.04 | 2.09 | 2.42 | 4.00 | 0.2038 |
| 46 | 67 | 1.07 | 0.45 | 2.64 | 2.13 | 2.06 | -- | -- |
| 47 | 67 | 0.94 | 0.38 | 5.48 | 2.23 | 2.90 | 4.58 | 0.1865 |
| 48 | 75 | 0.34 | 0.41 | 5.97 | 1.98 | 1.26 | 4.58 | 0.1072 |
| 49 | 54 | 1.49 | 0.91 | 2.69 | 2.87 | 2.83 | 4.00 | 0.2801 |
| 50 | 63 | 1.30 | 0.50 | 5.51 | 3.24 | 2.74 | 4.52 | 0.1535 |
| 51 | 66 | 1.32 | 0.96 | 3.60 | 2.00 | 2.09 | 4.63 | 0.1781 |
| 52 | 60 | 1.16 | 0.51 | 3.98 | 2.10 | 1.48 | 3.97 | 0.2801 |
| 53 | 67 | 2.22 | 1.48 | 2.82 | 3.31 | 3.19 | 4.00 | 0.2499 |
| 54 | 71 | 1.51 | 0.91 | 2.96 | 2.36 | 2.71 | 3.72 | 0.4767 |
| 55 | 60 | 1.08 | 0.73 | 2.09 | 1.89 | 2.07 | 3.68 | 0.3239 |
| 56 | 58 | 0.92 | 0.33 | 5.32 | 2.64 | 2.31 | 4.12 | 0.2127 |
| 57 | 49 | 1.49 | 0.78 | 3.70 | 3.10 | 3.10 | 4.73 | 0.3014 |
| 58 | 60 | 1.42 | 0.78 | 2.11 | 2.53 | 2.36 | 4.00 | 0.1616 |
| 59 | 62 | 0.69 | 0.39 | 5.10 | 1.87 | 1.85 | 3.95 | 0.1456 |
| 60 | 46 | 2.61 | 1.57 | 4.20 | 4.35 | 4.21 | 4.00 | 0.2309 |
| 61 | 59 | 3.20 | 2.33 | 4.19 | 5.24 | 5.29 | -- | 0.6160 |
| 62 | 60 | 2.11 | 1.22 | 3.51 | 3.91 | 3.55 | 4.00 | 0.2217 |
| 63 | 59 | 1.09 | 0.64 | 4.50 | 2.53 | 2.35 | 4.00 | 0.3602 |
| 64 | 43 | 1.35 | 0.78 | 3.10 | 2.69 | 2.54 | 3.88 | 0.1781 |

Appendix E-II. Report of statistical analysis of pulmonary function and forced oscillation data

Key to item listing:

Pre-bronchodilator therapy

| | |
|---|---|
| T13 | Total Pulmonary Resistance |
| T14 | Total Pulmonary Conductance |
| T15 | Maximum Mid-Expiratory Flow |
| T16 | Maximum Mid-Inspiratory Flow |
| T17 | Peak Expiratory Flow |
| T18 | Forced Vital Capacity |
| T19 | Forced Expiratory Volume (1 sec) |
| T20 | Vital Capacity |
| T21 | Functional Residual Capacity |

Post-bronchodilator therapy

| | |
|---|---|
| T22 | Total Pulmonary Resistance |
| T23 | Total Pulmonary Conductance |
| T24 | Maximum Mid-Expiratory Flow |
| T25 | Maximum Mid-Inspiratory Flow |
| T26 | Peak Expiratory Flow |
| T27 | Forced Vital Capacity |

Calculated ratios

| | |
|---|---|
| T29 | MMEF/PEF Pre |
| T30 | TPC/FRC Post |
| T31 | MMEF/PEF Post |
| T32 | TPC/FRC Pre |
| T33 | $FEV_1$/VC Pre |
| T43 | MMEF/FVC Pre |
| T44 | MMEF/FVC Post |

| | NORMALS | | | PATIENTS | | |
|---|---|---|---|---|---|---|
| ITEM | MEAN | SD | N | MEAN | SD | N |
| T13 | 5.2161 | 2.1547 | 44 | 9.7757 | 2.8897 | 7 |
| T14 | 0.2257 | 0.1041 | 44 | 0.1098 | 0.0303 | 7 |
| T15 | 2.6159 | 1.1390 | 44 | 1.0786 | 0.4594 | 7 |
| T16 | 2.7028 | 1.4163 | 43 | 2.0819 | 1.0053 | 7 |
| T17 | 3.8388 | 1.6411 | 43 | 2.3471 | 1.0117 | 7 |
| T18 | 2.2644 | 0.9830 | 43 | 1.7857 | 0.6036 | 7 |
| T19 | 1.8484 | 0.7576 | 43 | 1.1457 | 0.3988 | 7 |
| T20 | 2.3077 | 0.9514 | 44 | 1.8700 | 0.5670 | 7 |
| T21 | 1.3868 | 0.5719 | 44 | 1.6357 | 0.3936 | 7 |
| T22 | 4.8820 | 1.0202 | 3 | 6.5151 | 4.4814 | 5 |
| T23 | 0.2111 | 0.0454 | 3 | 0.2022 | 0.0967 | 5 |
| T24 | ************ | ************ | 2 | 1.6650 | 0.9030 | 5 |
| T25 | ************ | ************ | 2 | 2.0380 | 0.8368 | 5 |
| T26 | ************ | ************ | 2 | 2.5440 | 1.3363 | 5 |
| T27 | 1.4857 | 0.3011 | 3 | 1.8990 | 0.6954 | 5 |
| T29 | 0.6967 | 0.1372 | 43 | 0.4632 | 0.0895 | 7 |
| T30 | 0.1837 | 0.0090 | 3 | 0.1146 | 0.0405 | 5 |
| T31 | ************ | ************ | 2 | 0.6425 | 0.1112 | 5 |
| T32 | 0.1673 | 0.0474 | 44 | 0.0629 | 0.0235 | 7 |
| T33 | 0.7942 | 0.0926 | 43 | 0.6031 | 0.0484 | 7 |
| T43 | 1.2142 | 0.3758 | 43 | 0.5849 | 0.1239 | 7 |
| T44 | ************ | ************ | 2 | 0.8177 | 0.2525 | 5 |

T-TEST

| ITEM | T | DF |
|---|---|---|
| T13 | 4.9632 | 49 |
| T14 | 5.9640 | 33 |
| T15 | 3.9014 | 49 |
| T16 | 1.1115 | 49 |
| T17 | 2.3219 | 49 |
| T18 | 1.2443 | 49 |
| T19 | 2.3860 | 49 |
| T20 | 1.1665 | 49 |
| T21 | 1.1058 | 49 |
| T22 | 0.6034 | 6 |
| T23 | 0.1461 | 6 |
| T24 | ************ | *** |
| T25 | ************ | *** |
| T26 | ************ | *** |
| T27 | 0.9485 | 6 |
| T29 | 4.3328 | 49 |
| T30 | 2.1741 | 6 |
| T31 | ************ | *** |
| T32 | 5.2979 | 49 |
| T33 | 5.9241 | 49 |
| T43 | 8.5034 | 29 |
| T44 | ************ | *** |

CHILDREN

| | NORMALS | | PATIENTS | |
|---|---|---|---|---|
| ITEMS | R | N | R | N |
| T19-T18 | 0.95614 | 42 | 0.97760 | 7 |
| T15-T17 | 0.88919 | 43 | 0.87558 | 7 |
| T15-T20 | 0.79081 | 44 | 0.93410 | 7 |
| T15-T18 | 0.77015 | 43 | 0.92511 | 7 |
| T14-T21 | 0.79975 | 44 | 0.05436 | 7 |
| T32-T15 | 0.16297 | 44 | -0.17910 | 7 |
| T32-T43 | 0.42867 | 43 | 0.10514 | 7 |
| T14-T15 | 0.77291 | 44 | -0.02777 | 7 |
| T14-T19 | 0.76749 | 43 | -0.03976 | 7 |
| T32-T33 | 0.18419 | 43 | -0.19659 | 7 |
| T19-T27 | 0.98885 | 3 | 0.92385 | 5 |
| T24-T26 | *********** | 2 | 0.94706 | 5 |
| T24-T20 | *********** | 2 | 0.93714 | 5 |
| T24-T27 | *********** | 2 | 0.96254 | 5 |
| T23-T21 | -0.99024 | 3 | 0.77943 | 5 |
| T30-T24 | *********** | 2 | 0.88599 | 5 |
| T30-T44 | *********** | 2 | 0.79677 | 5 |
| T23-T28 | *********** | 1 | 0.84483 | 5 |
| T30-T33 | 0.83517 | 3 | 0.89652 | 5 |
| T23-T24 | *********** | 2 | 0.81181 | 5 |

| | NORMALS | | | PATIENTS | | |
|---|---|---|---|---|---|---|
| ITEM | MEAN | SD | N | MEAN | SD | N |
| T13 | 2.5193 | 1.1582 | 62 | 4.1697 | 2.0711 | 93 |
| T14 | 0.4696 | 0.1909 | 62 | 0.3045 | 0.1642 | 93 |
| T15 | 4.0284 | 1.4973 | 63 | 1.5575 | 1.2678 | 97 |
| T16 | 4.4581 | 1.7449 | 63 | 2.9720 | 1.5855 | 97 |
| T17 | 7.3186 | 2.0944 | 63 | 4.0738 | 2.0068 | 97 |
| T18 | 4.4633 | 1.2999 | 63 | 3.1615 | 1.0310 | 96 |
| T19 | 3.1373 | 0.9478 | 63 | 1.7974 | 0.8287 | 97 |
| T20 | 4.3583 | 1.2350 | 64 | 3.2540 | 1.0194 | 97 |
| T21 | 3.3939 | 0.8214 | 64 | 3.9051 | 1.1704 | 97 |
| T22 | 2.4894 | 1.1140 | 20 | 3.4195 | 1.8016 | 74 |
| T23 | 0.4833 | 0.2139 | 20 | 0.3578 | 0.1506 | 78 |
| T24 | 3.8552 | 1.2969 | 21 | 1.9762 | 1.4809 | 80 |
| T25 | 4.2400 | 1.7478 | 21 | 3.1485 | 1.5253 | 80 |
| T26 | 7.0067 | 2.0856 | 21 | 4.4099 | 1.9822 | 81 |
| T27 | 4.0967 | 1.0638 | 21 | 3.4571 | 0.8985 | 80 |
| T29 | 0.5607 | 0.1483 | 63 | 0.3592 | 0.1890 | 97 |
| T30 | 0.1401 | 0.0549 | 20 | 0.0990 | 0.0486 | 74 |
| T31 | 0.5682 | 0.1504 | 21 | 0.4194 | 0.1900 | 80 |
| T32 | 0.1397 | 0.0524 | 62 | 0.0876 | 0.0591 | 93 |
| T33 | 0.7258 | 0.0963 | 63 | 0.5427 | 0.1563 | 97 |
| T43 | 0.9219 | 0.2543 | 63 | 0.4692 | 0.3011 | 96 |
| T44 | 0.9548 | 0.2429 | 21 | 0.5552 | 0.3468 | 80 |

ADULTS (PATIENTS)

| | NON-OBS | | | OBSTRUCTIVE | | |
|---|---|---|---|---|---|---|
| ITEM | MEAN | SD | N | MEAN | SD | N |
| T13 | 2.9936 | 1.4951 | 31 | 4.7562 | 2.1085 | 62 |
| T14 | 0.4079 | 0.1975 | 31 | 0.2528 | 0.1154 | 62 |
| T15 | 2.9595 | 1.2952 | 33 | 0.9867 | 0.5638 | 64 |
| T16 | 3.6527 | 1.7579 | 33 | 2.6209 | 1.3759 | 64 |
| T17 | 5.4398 | 2.0992 | 33 | 3.3700 | 1.6147 | 64 |
| T18 | 3.5024 | 0.9547 | 33 | 2.9829 | 1.0315 | 63 |
| T19 | 2.4045 | 0.7347 | 33 | 1.4844 | 0.6925 | 64 |
| T20 | 3.5233 | 0.9930 | 33 | 3.1152 | 1.0125 | 64 |
| T21 | 3.2285 | 0.8790 | 33 | 4.2539 | 1.1539 | 64 |
| T22 | 2.7830 | 1.1486 | 23 | 3.7065 | 1.9717 | 51 |
| T23 | 0.4145 | 0.1482 | 23 | 0.3323 | 0.1459 | 51 |
| T24 | 3.3712 | 1.6264 | 26 | 1.3046 | 0.7791 | 54 |
| T25 | 3.8769 | 1.6724 | 26 | 2.7978 | 1.3278 | 54 |
| T26 | 5.9427 | 1.9952 | 26 | 3.6853 | 1.5266 | 55 |
| T27 | 3.6042 | 0.8769 | 26 | 3.3963 | 0.9082 | 54 |
| T29 | 0.5464 | 0.1777 | 33 | 0.2627 | 0.1027 | 64 |
| T30 | 0.1336 | 0.0496 | 23 | 0.0935 | 0.0396 | 51 |
| T31 | 0.5726 | 0.1958 | 26 | 0.3456 | 0.1365 | 54 |
| T32 | 0.1349 | 0.0704 | 31 | 0.0639 | 0.0334 | 62 |
| T33 | 0.6865 | 0.1025 | 33 | 0.4696 | 0.1245 | 64 |
| T43 | 0.8111 | 0.2385 | 33 | 0.2901 | 0.1215 | 63 |
| T44 | 0.9118 | 0.3163 | 26 | 0.3835 | 0.1991 | 54 |

### Normals vs All Patients

T-TEST

| ITEM | T | DF |
|---|---|---|
| T13 | 6.3362 | 149 |
| T14 | 5.7442 | 153 |
| T15 | 11.5311 | 159 |
| T16 | 5.5669 | 159 |
| T17 | 9.8416 | 159 |
| T18 | 7.0446 | 157 |
| T19 | 9.4382 | 159 |
| T20 | 6.1783 | 159 |
| T21 | 3.2548 | 159 |
| T22 | 2.1932 | 92 |
| T23 | 3.0062 | 92 |
| T24 | 5.3077 | 99 |
| T25 | 2.8304 | 99 |
| T26 | 5.2934 | 100 |
| T27 | 2.7919 | 99 |
| T29 | 7.1522 | 159 |
| T30 | 3.2646 | 92 |
| T31 | 3.2906 | 99 |
| T32 | 5.6258 | 153 |
| T33 | 9.1621 | 159 |
| T43 | 9.8457 | 157 |
| T44 | 4.9620 | 99 |

### Non-Obs vs Obs Patients

T-TEST

| ITEM | T | DF |
|---|---|---|
| T13 | 4.7903 | 84 |
| T14 | 4.0408 | 41 |
| T15 | 8.6509 | 39 |
| T16 | 3.1773 | 95 |
| T17 | 5.4929 | 95 |
| T18 | 2.4034 | 94 |
| T19 | 6.0729 | 95 |
| T20 | 1.8933 | 95 |
| T21 | 4.4751 | 95 |
| T22 | 2.5269 | 67 |
| T23 | 2.2319 | 72 |
| T24 | 6.1491 | 31 |
| T25 | 3.1239 | 78 |
| T26 | 5.6281 | 79 |
| T27 | 1.0163 | 78 |
| T29 | 8.4696 | 43 |
| T30 | 4.6484 | 72 |
| T31 | 6.0293 | 79 |
| T32 | 5.3231 | 37 |
| T33 | 8.6512 | 95 |
| T43 | 11.7744 | 41 |
| T44 | 7.8044 | 35 |

### Normals vs Non-Obs Patients

T-TEST

| ITEM | T | DF |
|---|---|---|
| T13 | 1.7318 | 91 |
| T14 | 1.4528 | 91 |
| T15 | 4.0201 | 94 |
| T16 | 2.1425 | 94 |
| T17 | 4.2485 | 94 |
| T18 | 3.7715 | 94 |
| T19 | 3.8703 | 94 |
| T20 | 3.3612 | 95 |
| T21 | 0.9176 | 95 |
| T22 | 0.8476 | 41 |
| T23 | 1.2397 | 41 |
| T24 | 1.1110 | 45 |
| T25 | 0.7253 | 45 |
| T26 | 1.7850 | 45 |
| T27 | 1.7403 | 45 |
| T29 | 0.4197 | 94 |
| T30 | 0.4123 | 41 |
| T31 | 0.0843 | 45 |
| T32 | 0.3702 | 91 |
| T33 | 1.8572 | 94 |
| T43 | 2.0698 | 94 |
| T44 | 0.5124 | 45 |

### Normals vs Obs Patients

T-TEST

| ITEM | T | DF |
|---|---|---|
| T13 | 7.3216 | 95 |
| T14 | 7.6541 | 102 |
| T15 | 16.4660 | 81 |
| T16 | 6.5943 | 125 |
| T17 | 11.9451 | 125 |
| T18 | 7.1196 | 124 |
| T19 | 11.2073 | 113 |
| T20 | 6.2273 | 124 |
| T21 | 4.8576 | 114 |
| T22 | 3.2727 | 69 |
| T23 | 3.4196 | 69 |
| T24 | 8.4971 | 26 |
| T25 | 3.8544 | 73 |
| T26 | 7.6346 | 74 |
| T27 | 2.9973 | 73 |
| T29 | 13.1494 | 112 |
| T30 | 4.8433 | 89 |
| T31 | 6.0328 | 73 |
| T32 | 9.5969 | 104 |
| T33 | 13.0085 | 125 |
| T43 | 17.7913 | 89 |
| T44 | 10.4801 | 73 |

| ITEMS | R | N | R | N |
|---|---|---|---|---|
| T19-T18 | 0.77570 | 63 | 0.84385 | 96 |
| T15-T17 | 0.66302 | 63 | 0.75491 | 97 |
| T15-T20 | 0.60045 | 63 | 0.54598 | 97 |
| T15-T18 | 0.56322 | 63 | 0.60145 | 96 |
| T14-T21 | 0.43598 | 62 | -0.13497 | 93 |
| T32-T15 | -0.00805 | 61 | 0.46744 | 93 |
| T32-T43 | -0.10855 | 61 | 0.55276 | 92 |
| T14-T15 | 0.16015 | 61 | 0.50989 | 93 |
| T14-T19 | 0.47237 | 61 | 0.52813 | 93 |
| T32-T33 | 0.20231 | 61 | 0.61299 | 93 |
| T19-T27 | 0.96347 | 21 | 0.73234 | 80 |
| T24-T26 | 0.70670 | 21 | 0.77177 | 80 |
| T24-T20 | 0.51765 | 21 | 0.53297 | 80 |
| T24-T27 | 0.59641 | 21 | 0.49021 | 80 |
| T23-T21 | 0.43879 | 20 | 0.00581 | 74 |
| T30-T24 | 0.15222 | 20 | 0.46580 | 73 |
| T30-T44 | 0.17949 | 20 | 0.54063 | 73 |
| T23-T28 | 0.27575 | 16 | 0.68179 | 39 |
| T30-T33 | 0.00201 | 20 | 0.61587 | 74 |
| T23-T24 | 0.12905 | 20 | 0.46487 | 73 |

ADULTS (PATIENTS)

| | NONOBSTRUCTIVES | | OBSTRUCTIVES | |
|---|---|---|---|---|
| ITEMS | R | N | R | N |
| T19-T18 | 0.90055 | 33 | 0.85533 | 63 |
| T15-T17 | 0.61212 | 33 | 0.80200 | 64 |
| T15-T20 | 0.59954 | 33 | 0.73735 | 64 |
| T15-T18 | 0.68170 | 33 | 0.73921 | 63 |
| T14-T21 | 0.26259 | 31 | -0.03019 | 62 |
| T32-T15 | -0.04019 | 31 | 0.39364 | 62 |
| T32-T43 | 0.14246 | 31 | 0.33662 | 61 |
| T14-T15 | 0.22087 | 31 | 0.44347 | 62 |
| T14-T19 | 0.21119 | 31 | 0.56817 | 62 |
| T32-T33 | 0.25809 | 31 | 0.55350 | 62 |
| T19-T27 | 0.89235 | 26 | 0.76477 | 54 |
| T24-T26 | 0.63605 | 26 | 0.73613 | 54 |
| T24-T20 | 0.57904 | 26 | 0.55263 | 54 |
| T24-T27 | 0.69065 | 26 | 0.50561 | 54 |
| T23-T21 | 0.43925 | 23 | 0.01630 | 51 |
| T30-T24 | 0.10336 | 23 | 0.43680 | 50 |
| T30-T44 | 0.28651 | 23 | 0.38080 | 50 |
| T23-T28 | 0.63429 | 13 | 0.64077 | 26 |
| T30-T33 | 0.38965 | 23 | 0.50764 | 51 |
| T23-T24 | 0.48920 | 23 | 0.39744 | 50 |